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MALIGNANT MELANOMA IN THE NEGRO*

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Benign and malignant pigmented tumors are rare in the negro. In an exhaustive search through the literature only two cases of malignant melanoma were found, and correspondence with a number of dermatologists in the southern part of the United States reveals the fact that it is an uncommon disease, many observers never having seen a case. Only five reports were collected and these are included in this paper. Stevenson [1] has reported eighteen cases of melanoma in Hindus, all but three of which originated on the sole or heel. A history of trauma was obtained in each instance, there being the additional fact that the Hindus usually go barefooted.

The normal dark pigmentation of the skin in the colored race makes an early diagnosis difficult. Malignant melanotic tumors usually exhibit themselves as nodules adjoining a primary nodule or mole or as metastatic nodules elsewhere in the body. In this case, the extensive uniform pigmentation which is contrary to the rule obscured the true condition. Malignant melanoma can occur at any age, but it is rarely seen before the age of 15 years or after 80. It is particularly likely to start from a birthmark, mole or wart, around the nails on the fingers or toes, or the dark skin about the nipple, external genitalia, and anus. Cases are on record of melanoma originating in almost every organ of the body. Although our patient gave no definite history of a primary mole or nevus, a dog had bitten her in the region of the primary lesion. Trauma is considered a likely exciting cause of this type of tumor, especially when applied to a pigmented nevus. The point is emphasized by Wilson and Kalteyer [2] in their analytic study of sarcomas of the skin.

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1. Stevenson, W. H. D.: Malignant Melanomata: Especially Those Occurring on the Heel and Sole of the Foot, Indian J. M. Res., **3**:166, 1915.

2. Wilson, J. C., and Kalteyer, F. J.: Report of a Case of Sarcomatosis Cutis, Together with an Analytical Study of Fifty Other Cases Collected from the Recent Literature, Am. J. M. Sc. **126**:751, 1903.

While no extensive statistics have ever been compiled, it is the belief among many observers that skin diseases are less common in the negro than in white people, although they suffer more from disease in general. Fox [3] states that epithelioma is less common in the negro, yet the negro is more susceptible to new growths of connective tissue origin. Nevertheless, in the thousands of cases reviewed, he does not mention a case of malignant melanotic tumor. It has been observed as a corollary to its incidence in the black and white races of man that malignant melanotic tumors are more common in white and light colored horses than in dark ones.

Aside from the fact that this type of neoplasm in a negro is so rare, the subject presents many interesting problems, some of which we shall present and discuss.

REPORT OF A CASE

History.—M. B., a negress, aged 78, a widowed housewife, was referred to the Albany Hospital by her family physician on Dec. 12, 1921, presenting as her complaint a markedly swollen and cumbersome left lower extremity. There had been intermittent dull aching pains in the left leg and foot since the early spring of 1921. The family history was negative. There had been a loss of weight of 50 pounds (22.6 kg.) since 1918, when the patient had weighed her best, 180 pounds (81.6 kg.), her present weight being 130 pounds (58.9 kg.). The most striking loss that she noticed had taken place since June, 1921. Her general health had always been excellent. She spoke of having been bitten by a dog nine years before on her left small toe and foot, and again of having injured the same foot three years before by tripping on the stairs.

There was no history of venereal infection.

Present Illness.—The patient's attention was first attracted to her left extremity by the development of dull aching pains in her left foot during the early part of June, 1921. At first the pains seemed to be "just in the skin" of the foot, and were intermittent. Her attention being thus drawn to her foot, she was struck by the fact that her foot was getting black. At the same time she noticed a swelling of the foot and ankle, the swelling gradually reaching the knee. The pain also ascended, involving now the foot, the knee and the thigh. It became so constant that the patient had to sit up in bed at night and rub the leg with camphorated oil. Slowly the swelling began to involve the thigh; but there was no pain above the knee. Suddenly she noticed that her leg was getting hard. This frightened her. The swelling kept increasing. At times, after the pain began to ascend in the leg, the knee was the most painful part. Yet the foot, especially in the region of the lateral toes, was the most tender. While rubbing her leg one day with oil, she noticed that the blackness in her foot had spread to her ankle. It was also appearing as little round spots on her leg; the patient described them as looking like "black freckles." In places she noticed that they ran together. Small blisters on the ankle and foot attracted her attention next. These would break and form small scabs. The dressings quickly became saturated with serum from the leg. The continued saturation of the cloths after being on only for a short time was discouraging.

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3. Fox, Howard: Observations on Skin Diseases in the Negro, J. Cutan. Dis., February, 1908.

she said, and gradually she began to neglect her treatment. What struck her in changing the dressings was the large flakes of skin adhering to the linen. She could peel these thin flakes from her leg in pieces 1 to 2 inches in length.

She did not notice any great swelling of the thigh until five weeks before her entrance into the hospital, and the swelling was brought to her attention by a physician whom she went to see regarding the soreness and development of large blisters on the outer side of her left foot.

One week before entrance into the hospital, a visiting nurse while changing the dressings on the patient's leg told her that her little toe had fallen off into the dressings. The patient laid the incident of the dropping off of her toe to the result of the dog bite received nine years before.

At no time during the development of the swelling in the leg did the patient feel any illness or weakness, nor was she unable to walk about.

Physical Examination.—The patient was a frail elderly woman of average intelligence, who showed signs both of mental and physical senility. The skin was chocolate brown, satiny, dry and wrinkled, and fell into large folds over the lateral abdominal and iliac regions. There was a general looseness of the skin, suggesting loss of subcutaneous fat. The flesh throughout was flabby, except in the left leg which was boardlike.

Bilateral arcus senilis, lens opacity and tortuosity of the retinal arteries were present. The pupils were equal and reacted consensually to light and accommodation. The ocular movements were normal. Hearing was slightly impaired. There was no pigmentation or discoloration of the mucous membrane of the mouth, lips or nose. Only the inguinal and femoral lymph glands were palpable. There was nothing striking in the chest, except a slightly enlarged heart.

The radial vessels seemed about twice their normal size, and were tortuous and beaded. The temporals, the right posterior tibial, and the axillary arteries were likewise enlarged and firm. The brachial artery could be seen beating in the cubital space. Generally the pulse tension was high. The blood pressure was 240 systolic, 140 diastolic.

There was great looseness of the skin and laxity of the abdominal wall. On percussion, the liver dulness began at the fifth rib and reached 6 cm. below the right costal margin. An examination made five weeks later showed that it extended 8 cm. below the right costal arch. Its edge was smooth at both times.

A rectal examination was negative. Generally the cutaneous and tendon reflexes were present and active. The musculature of both arms and of the right leg was atrophic.

The left lower extremity showed tremendous swelling from the pelvis to the toes. The black thick skin gave the impression that the limb was made of hard black rubber. The color was a dusky black in contrast to the chocolate brown of the patient's normal skin. Where it was most intense, in the lower leg and foot, the skin was much indurated, so that to the touch it gave the impression of thick paper saturated with tar. This brawniness extended to the junction of the middle with the upper third of the thigh, being more marked on its anterior and lateral aspects. Above this level the blackness took on a speckled appearance, giving a picture of scattered black dots varying in size from 1 to 3 mm. These small dots faded out and disappeared in the proximal part of the thigh, the skin in this area being normal in color. There were places in which the dots could be seen blending.

A peculiar roughness was imparted to the skin by the presence of scattered multiple broken areas, resembling ulcers, oval, round, irregular or linear in shape, most thickly located on the dorsal aspect of the foot and on the anterior surface of the ankle and lower leg. They appeared to be ruptured areas in the skin, having raised jagged edges, and discharging a serous fluid. The most remarkable one appeared as a linear tear in the skin stretching from the heel to the distal end of the fifth metatarsal bone, where it ended at a moist gangrenous-like stump which was all that remained of the small toe. It was in this region on the dorsum of the foot that a small isolated black nodule was noted; it was distinctly raised above the surface of the foot. All the toes were increased in size and deeply pigmented, with the exception of the great toe, the normal color of which stood out strangely in contrast with that of the blackened foot.

Throughout the extremity where the abnormal blackness was present, the epidermis flaked off in irregular thin gray scales. They were thickly scattered over the surface of the dressings.

The left thigh at the level of the greater trochanter measured 65 cm. in circumference, and at the point just above the patella, 49.5 cm. The same circumferences of the opposite thigh were 46 cm. and 34 cm. respectively. There was a difference of 19 cm. in circumference between the two thighs at the level of the greater trochanters.

The inguinal glands were enlarged in both sides. On the left they were about 3 cm. and on the right about 2 cm. in size. The femoral glands, which could be palpated only on the right, were about the size of small peas. They were all hard, but none was tender.

There was no marked impairment of motion in the leg, but the impression was given of the patient's having to move a heavy leg. Hyperesthesia and hyperalgesia of the toes and foot were present.

Examination of the blood revealed: hemoglobin, 80 per cent. (Dare); erythrocytes, 4,500,000; leukocytes, 11,600; and a lymphocytosis of 45 per cent. These findings remained fairly constant throughout the patient's stay in the hospital.

The urine was amber, and the specific gravity between 1.015 and 1.020. Examination for sugar was negative. A trace of albumin was persistent. The microscopic examination was negative. Fresh and twenty-four hour specimens repeatedly allowed to stand for forty-eight hours never revealed melanin macroscopically. The addition of ferric chlorid gave a gray precipitate which blackened on standing. This is not a conclusive test for melanin but is suggestive of its presence.

Two blood Wassermann reactions were negative. The roentgen-ray examination of the chest showed no evidence of metastasis to the lungs.

Operation.—The day following the patient's entrance into the hospital, the left extremity was successfully amputated under spinal anesthesia at the level of the middle of the thigh.

Surgical Specimen.—The specimen consisted of the left leg amputated 16 cm. above the knee joint at the junction of the middle and lower thirds of the femur. The whole leg was swollen, moist and edematous. The specimen measured approximately 65 cm. in length and 45 cm. in circumference at the calf. On first inspection, the striking thing was the intense pigmentation of the entire leg with the exception of an area on the plantar surface of the heel measuring 7 by 5 cm. and extending up over the posterior aspect of the heel

for a distance of 2 cm. where there were a few scattered deeply pigmented areas varying in size from 0.1 cm. to 1 cm. in diameter. The great toe showed only a normal negroid pigmentation, as did the greater part of the ball of the foot. Toward the periphery of all of these nonpigmented areas there appeared scattered black punctations which became more numerous and finally fused with the intense pigment of the rest of the leg. The remainder of the sole was jet black, except for scattered areas of superficial epidermis which were grayish and flaked off leaving a similar black surface underneath.

Over the greater part of the foot, ankle and particularly the lateral aspect of the lower third of the leg were numerous irregularly shaped grayish vesicles, apparently located under the superficial layers of the epidermis. They were fluctuant, filled with a clear fluid and varied in size from 0.1 to 1 cm. in diameter. They were fairly well limited by the retinacula of the skin. Many of these vesicles had ruptured, forming small superficial ulcerations around which the skin was indurated and contracted, the same black pigment, however, underlying all of the vesicles. This condition of the skin is well shown in Figures 1 and 3.

The skin of the entire leg felt markedly thickened and indurated, having about the consistency of gutta percha.

Fig. 1.—Body of negress, the authors' patient, at necropsy, showing the well-healed stump, the pitch black pigmentation and swelling of the left thigh.

The fifth toe was absent, and about its former site was an area of moist necrosis. A tendon projected 0.5 cm. from a depressed area at the former site of the fifth toe. Bordering the tendon were three or four polypoid projections, one being about 3 by 4 by 3 mm., and another, which may have been a part of the stump of the fifth toe, measuring 1 by .7 by 1 cm. These masses on section were black and of fibrous consistency, suggesting old pigmented granulation tissue. At about the base of the fourth toe, on the dorsal surface, was a circumscribed ovoid raised mass about 3 by 2 cm. and raised above the surface about 6 mm. The surface was smooth, brownish black and on section black and fibrous.

Section through the skin at many levels showed it to be greatly thickened, indurated and black. The pigmentation extended downward into the subcutaneous tissue a distance of from a few millimeters to 2.5 cm., being greatest over the foot and ankle, especially over the lateral surface, where it extended down to the periosteum, and thinned out toward the proximal end of the leg. There was some irregular yellow mottling of fat in the pigment of the subcutaneous tissues. There were areas of more normal brownish skin about the knee, and section of these and of the skin over the great toe showed absence of this extraneous pigment.

The popliteal artery showed a moderate amount of sclerosis, and there was some thickening of the walls of the accompanying veins.

Dissection of the leg showed a tremendous infiltration by the black pigment. It was most intense in the skin and subcutaneous tissue throughout the entire extremity. It had infiltrated along the fascial planes, both superficial and deep, and in many cases into the connective tissues and surrounding the muscle

Fig. 2.—A posterior dissection of the leg showing the widespread distribution of the pigmented tumor in the skin, subcutaneous tissues, fasciae, muscle and tendon sheaths.

bundles. It was especially marked about the blood vessels, large and small, so that on cross section the blood vessels could often be picked out densely encased in black pigment. In many cases the walls of the blood vessels had been infiltrated and extension through into the lumen by this black pigmented

tissue had resulted. Lymphatics, nerve sheaths, nerves, tendon sheaths, tendons, in fact all the tissue in the leg including the bone marrow, was at some place infiltrated with this pigment. Figure 2 shows very well this extreme condition.

Dissection of the blood vessels downward showed first that the popliteal artery was surrounded by pigment. Some of the smaller vessels about the knee, as for instance the inferior medial geniculate, were deeply embedded in

Fig. 3.—The sole with the intracutaneous extension of the tumor and the moth-eaten appearance due to flaking of the epidermis. The big toe, ball and heel were comparatively free from pigment.

tumor. About 8 cm. below the knee the anterior and posterior tibials and the peroneal arteries and veins were deeply inlaid in tumor. In general the most superficial vessels in the skin and the deep vessels were more involved than those between these levels. In tracing the blood vessels downward to the

annular ligament the amount of pigment increased. At some levels the blood vessels seemed to be almost occluded by tumor; at others the lumen appeared quite patent although entirely surrounded by tumor.

As the anterior tibial emerged from under the annular ligament as the dorsalis pedis, it was devoid of any pigment. The lateral portion of the arcuate vessels and the branches which supplied the great and two adjoining toes were free, and this probably accounts for the lessened amount of pigment and absence of gangrene in this area. The vessels of the fourth and fifth toes, and the metatarsal arteries from the plantar arch on the sole of the foot supplying this area were practically occluded by atheroma and calcified material.

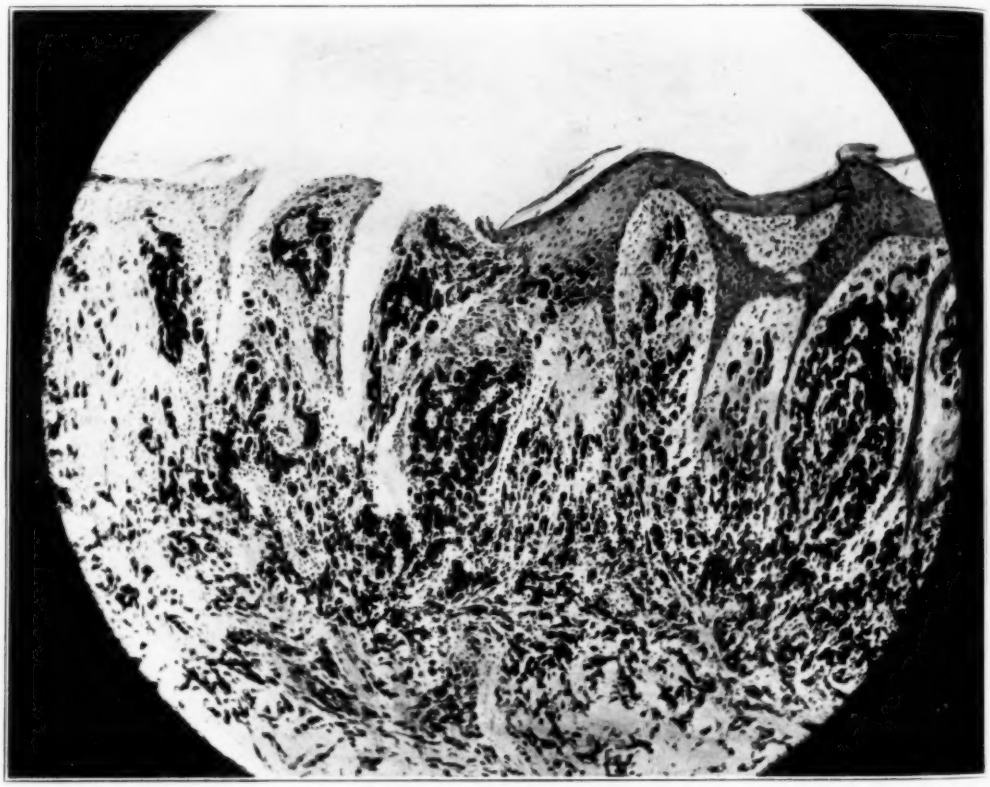

Fig. 4.—Photomicrograph of the skin from the sole close to the stump of the small toe. This area was quite similar to others much farther removed in the foot and also in the leg. Cells of various types laden with pigment were present in all layers of the skin and subcutaneous tissues.

The explanation suggested is that the tumor originated in the region of the fourth and fifth toes and that the blood vessels supplying this area were first invaded, causing thrombosis and leading to gangrene, for which condition the patient entered the hospital. The tumor then gradually spread over the lateral surface of the foot and ankle and so on to involvement of the whole leg. The posterior tibial and peroneal arteries near their terminations about the ankle joint were also less affected suggesting that they had been invaded higher up

in the leg in the course of the general upward extension of the tumor. The fact that the skin overlying these areas was more involved possibly can be explained by the fact that the tumor traveled more rapidly in the loose areolar and subcutaneous tissue which offered less resistance.

Histologic Examination.—Femoral Artery: There was much sclerosis with moderate concentric narrowing of the lumen. The vessel was surrounded by a growth of pigmented tumor cells which had spread diffusely in the areolar tissue and also in the perivascular sheath and lymph vessels.

Femoral Nerve: A section showed thickening of the perineurium but no tumor.

Popliteal Artery: The adventitia and media were invaded by pigmented tumor cells in great numbers. The lumen was greatly narrowed by intimal thickening.

Anterior Tibial Artery: In the midlevel of the leg it was embedded in tumor which formed a thick black collar about it and several medium sized veins accompanying it. The lumen was reduced to a narrow slit by thickening of the intima and there was considerable calcification in the media. Some tumor cells had invaded the vessel from the outside as far as the intima.

At the level of the annular ligament the artery was entirely occluded by a sclerotic process. The surrounding connective tissue with its nerves, lymph and venous channels, was heavily infiltrated with pigmented tumor.

Foot: The rounded elevation at the site of the little toe consisted of granulation tissue in which were large numbers of pigmented tumor cells of many sizes and shapes. Invasion of blood and lymph vessels and nerves had occurred in and about this growth. The adjacent epidermis was superficially ulcerated and many pigmented cells were enmeshed in the fibrin which lined the floor of the ulcer. The epidermis had been invaded by many polyhedral pigmented cells from the corium. These cells were without prickles and were easily distinguished from the squamous epithelium. The malpighian layer contained a normal amount of pigment for a negro, and in some places on the soles this layer was devoid of pigment. In the corium and subcutaneous tissues pigmented polyhedral cells were growing in every direction, often with a definite alveolar arrangement. It is impossible to say where the tumor took origin. No isolated nevus was found, but sections of the skin from several different portions of the dorsum and sole of the foot in the region of the fourth and fifth toes showed a condition which suggested that the chromatoblasts in these several loci may have undergone a malignant change in situ, then invaded the deeper tissues, blood and lymph vessels, and metastasized in the subcutaneous lymphatics to the rest of the leg, thus accounting for the diffuse pigmentation of the affected limb. The blood vessels showed marked obliterative changes, and the loss of the fifth toe was undoubtedly due to true "dry" gangrene, but there was no gangrene of the foot even though the anterior tibial artery was entirely occluded at the annular ligament.

Second Admission.—The patient left the hospital with a perfectly healed stump after having been about the hospital on crutches for a week before discharge (Jan. 28, 1922). Nothing was heard from her until her appearance at the hospital again on June 27, 1922. On this day she presented a most remarkably changed picture, being feeble and helpless. She desired no food nor attention, and suffered no pain. In the months which had elapsed she had wasted, her features being drawn and pinched. She had had no pain since the amputation of her leg, and all that she could give in her subjective history

was that she felt herself gradually getting weaker, that her appetite failed, and that her abdomen began to enlarge about six weeks after she had left the hospital.

She was emaciated. Her heart and lungs were negative. The liver dulness reached to the umbilicus. The abdomen was moderately distended, and gave signs of free fluid. The amputation stump was well healed. It was coal black, moist and looked as if it had been dipped in black paint. A towel rubbed over the stump could be made as black as the stump itself. The pigmentation had ascended to the top of the crest of the ileum posteriorly, and above the

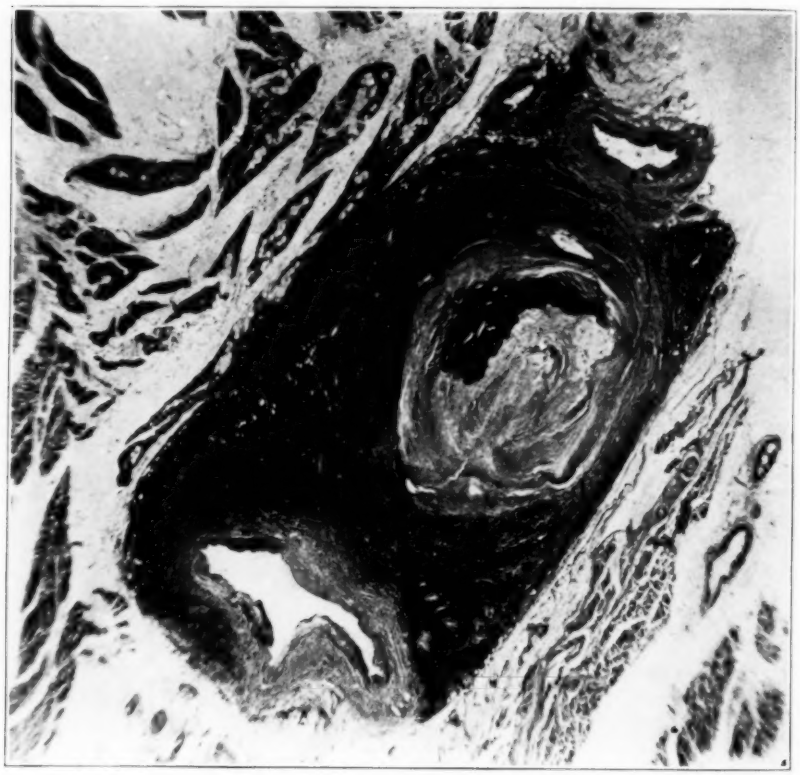

Fig. 5.—Photomicrograph of a section of the anterior tibial artery at the level of the annular ligament. It is entirely occluded by atheromatous and calcified material, and with its vena comites is almost completely encased in tumor.

pubic bone anteriorly, involving the external genitalia to the median line on the left. Small spots of pigment appeared on the anterior abdominal wall reaching toward the umbilicus. The abdomen and perineum to the right of the median line and the right leg were normally pigmented.

The blood showed a leukocyte count of 16,000, of which 32 per cent. were lymphocytes, and an erythrocyte count of 3,200,000. The hemoglobin content was 60 per cent. (Dare).

Four days after her entrance into the hospital, the patient developed bronchopneumonia and subsequently went into coma. She died on July 5, 1922, eight days after entrance.

Necropsy Examination.—Necropsy was performed six hours postmortem. The anatomic diagnosis was: (1). Malignant melanoma, primary in the left lower extremity, involving the skin and deep tissues as high as the inguinal ligament by direct extension. There were metastatic nodules in the liver, lungs, heart, spleen, kidneys, suprarenals, bone marrow, retroperitoneal and mediastinal lymphatics and lymph nodes. (2) Chronic fibrous myocarditis; (3) arteriosclerosis; (4) amputation stump of the left thigh, and (5) leiomyoma uteri. The microscopic diagnosis was: (1) acute bronchopneumonia; (2) hyperplasia of the suprarenal cortex; (3) chronic diffuse fibrous pancreatitis; (4) chronic vascular nephritis (arteriosclerotic), and (5) secondary anemia.

The body was that of an emaciated negress of medium shade and fair development. The left leg had been amputated about 10 cm. above the knee. The stump was well healed. The skin over the stump and over an area extending from 1 to 3 cm. above the inguinal ligament was coal black, shiny and moist, having the consistency of hard rubber. Fine rootlike projections extended from the edge of the pigmented area out into the normal skin. The pigmentation extended to and partly covered the left labium majus. On section, streaks of jet black tissue were seen running throughout the subcutaneous and deep tissues of the left thigh. Coal black enlarged lymph nodes were found along the course of the femoral vessels, the largest from 2.5 to 3 cm. The circumference of the stump of the right thigh was approximately one half again as great as that of the right thigh at corresponding levels.

The peritoneal cavity contained 200 c.c. of turbid straw colored fluid. There were numerous old fibrous adhesions binding the convex surface of the liver to the diaphragm. The omentum was adherent to the lower border of the liver. A few of the mesenteric lymph nodes were enlarged (from 0.5 to 0.6 cm.) and black. The retroperitoneal lymphatics and lymph nodes were clearly marked out by tumor, appearing as though injected with black fluid. There were a few tiny black tumor nodules scattered over both surfaces of the diaphragm.

About the bifurcation of the trachea and along the aorta were many small and large lymph nodes, of moderately firm consistency. On section, the cut surfaces were found to be black, firm and elastic.

The left pleural cavity contained 300 c.c., the right 400 c.c., of clear straw colored fluid.

The pericardial cavity contained 100 c.c. of clear yellowish fluid.

The heart weighed 480 gm. There were numerous small grayish scars scattered through the wall of the left ventricle. There were several small black tumor nodules, one 1 mm. in diameter beneath the epicardium covering the right auricle, another of similar size on the surface of the pulmonary artery, one 2 mm. in diameter within one of the columnae carneae of the right ventricle, and another 2 mm. in diameter within the left ventricular wall. The coronary arteries showed marked sclerosis and calcification. The valves appeared normal.

The right lung weighed 520 gm., the left 600 gm. They were crepitant. Over the surface and throughout the lung tissue were scattered many black nodules, varying in size from 0.1 to 0.7 cm. The cut surfaces were rather moist.

The spleen weighed 150 gm. Scattered throughout were numerous small black nodules of tumor, the largest being 5 cm. in diameter.

In the pancreas, the capsular lymphatics were injected with black material. The parenchyma of the organ appeared to be normal.

The liver weighed 1,700 gm. It contained many black tumor nodules, varying in size, the largest being 2 cm. in diameter.

The gallbladder was distended with bile, which was readily expressed through the ampulla on slight pressure. Close to the beginning of the cystic duct there was a lymph node 0.5 cm. in diameter, which was quite black.

The kidneys weighed 260 gm. each. The capsule stripped from each with some difficulty, leaving a coarsely granular surface. Both renal arteries were sclerotic. There were a few small scattered tumor nodules in each kidney, none over 0.2 cm. in diameter.

The suprarenals showed a few black tumor nodules from 0.1 to 0.2 cm. in diameter in the cortex.

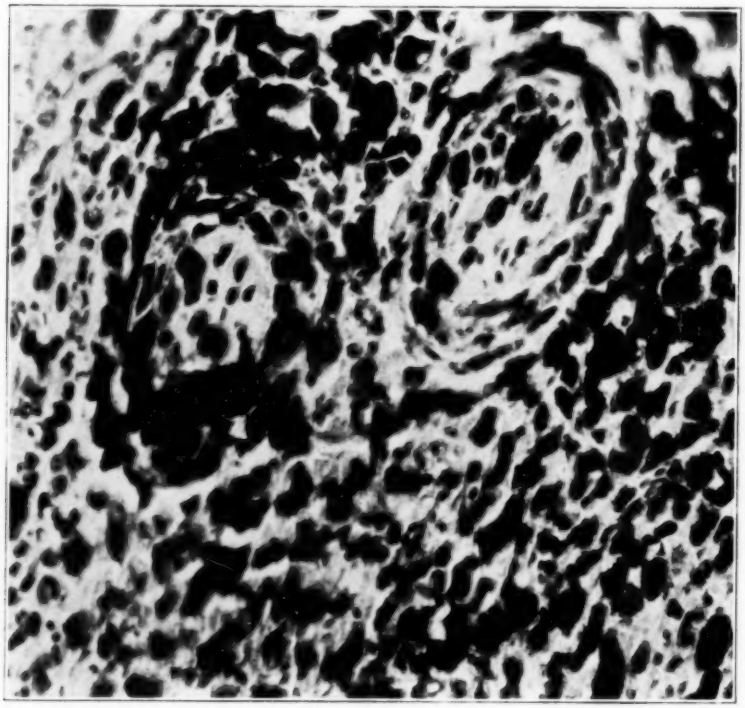

Fig. 6.—Invasion of nerve trunks of the leg by melanotic tumor.

The wall of the urinary bladder was diffusely invaded by tumor. The uterine wall and endometrium were diffusely invaded by tumor tissue. The lymphatics beneath the serosa of the tubes showed tumor metastases. There appeared to be involvement of the cortex of each ovary.

The intima showed numerous large irregular atheromatous patches with areas of calcificaion. Theses changes were most intense along the abdominal aorta. Throughout its length the aorta was surrounded by enlarged firm lymph nodes which had been invaded by tumor.

The bone marrow of the ribs and left femur was black and firm.

Microscopic Examination.— In the heart there was no tumor in three sections through different parts of the right and left ventricle walls. The

coronary arteries showed marked arteriosclerosis and narrowing. In the myocardium of the left ventricle and papillary muscles were fairly numerous foci of acute degeneration comprising about twenty fibers, but with no cellular reaction. There were numerous areas of fibrosis involving a few fibers and others much more extensive. The muscle fibers remaining were definitely hypertrophied, especially about the larger fibrous scars. The endocardium and pericardium were not remarkable. In one section a mass of pigmented tumor cells lay just beneath the endocardium of a columna carneae of the left ventricle.

In the lungs, subpleural metastases of tumor were present, the largest being 5 by 2 mm. From these nodules many dilated lymph channels led, and these often were filled with melanin-laden cells. The subjacent alveoli contained many polyhedral cells whose cytoplasm was quite filled with melanin in fine and coarse granules. Some cells in the alveoli contained yellowish brown hemosiderin. There were also small areas of acute bronchopneumonia and atelectasis.

In the spleen, the capsule was normal. Many fairly well circumscribed collections of tumor were present. They were grouped chiefly about the trabecular vessels and replaced many malpighian bodies. The tumor cells varied much in shape, but many were coarse spindle cells which often tended to grow in a concentric manner. The pigment content of these cells varied greatly, many containing practically none in the fixed preparation. It seems probable that the lipoid solvents, such as alcohol and chloroform, dissolved some of the pigment. This has been observed to occur by Dyson. There was much hyalinosis of arteries and an increased amount of hemosiderin in cells in the sinuses and pulp spaces.

In the liver were many metastatic tumor masses scattered throughout the organ. The metastases varied in size from single cells in branches of the portal vein to areas of closely packed cells 4 mm. in diameter. In the larger portal branches were also numerous pigmented cells, polyhedral and spindle. These cells resembled the tumor cells seen in other organs. The central portion of the cell was finely granular, the granules often being concentrated about the nucleus, in which similar pigment could be seen. The nucleus was shaped along the lines of the cell, being ovoid in the spindle cells and round or polyhedral in those of such proportions. Conspicuous everywhere in the sections was the phagocytosis of melanin by the Kupffer cells of the liver sinuses. These cells contained many very fine sharp black granules. The Prussian blue test revealed a very small amount of hemosiderin in a few liver cells here and there, but none in Kupffer cells. Mononuclear phagocytes were abundant in many portal areas in the loose connective tissue spaces, and these frequently contained coarse melanin granules. There was no increased fibroplasia in the liver, however. Acute congestion was present and several microscopic areas of hemorrhage of irregular distribution as regards their position in the lobule.

In the esophagus, there was no pigment present in the basal layers of the mucosal epithelium. The lymphatics of the submucosa were filled with tumor. The blood vessels showed much obliterative endarteritis.

A section of the colon was normal. A lymph node in the mesocolon was heavily infiltrated with tumor, many of the pigmented cells being of a large spindle type, about 60 microns in length, having fibrillary processes and appearing more like fibroblasts, especially those in the capsule.

In the pancreas marked arteriosclerosis and chronic diffuse fibrous pancreatitis were present. Many ectatic lymph vessels were present in the interlobar tissue. A lymph node attached to the capsule contained much tumor tissue, as did the small veins in the region of this lymph node.

In the suprarenals, tumor cells were present in large numbers in the veins and lymph vessels of the capsule. Melanin granules were also present in many fibroblasts in different parts of the capsule. In several places, the epithelial cells of the zona glomerulosa had undergone marked proliferation, having invaded the capsule and even the overlying fat. The cells, however, were of normal morphology, and while not forming well defined columns, they were easily recognized as suprarenal cortical epithelium. In the zona glomerulosa and zona fasciculata there was a great excess of lipoid. In the zona reticularis

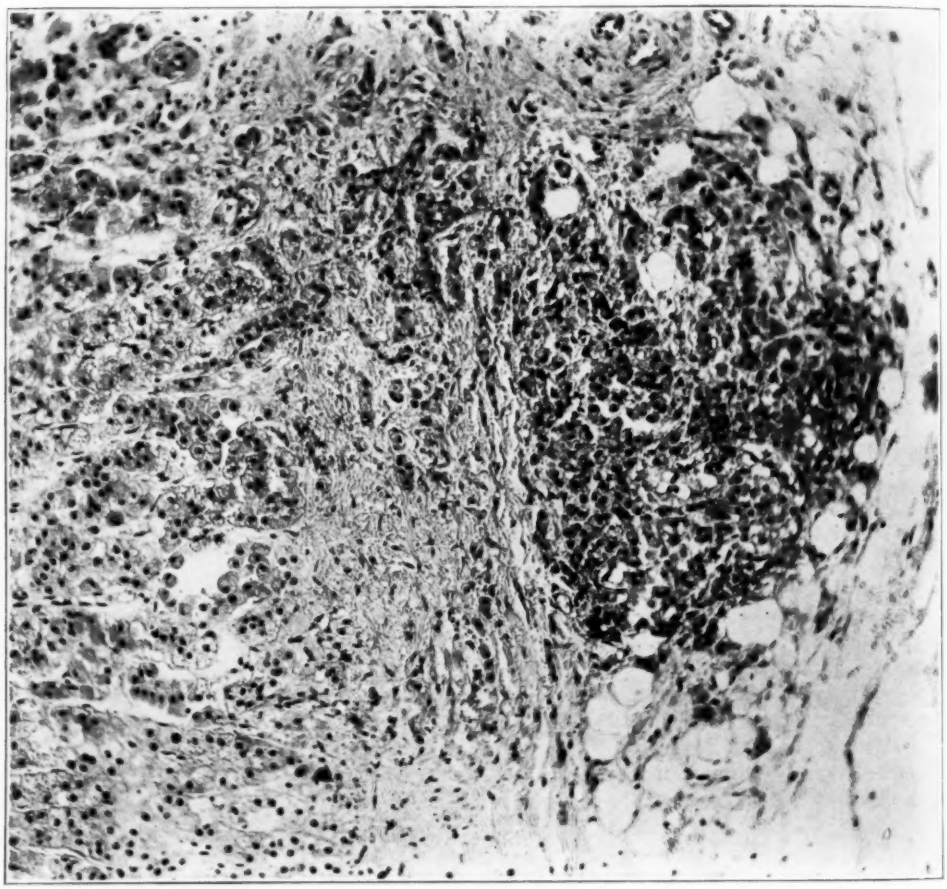

Fig 7.—Photomicrograph showing the hyperplasia and extension of cells of the suprarenal cortex into the capsule and adjacent fat.

melanin pigment, such as is usually seen in the aged, was present in normal amount. The arteries showed marked sclerosis. In the medulla were a few small lymphocytic foci.

In the uterus, the mucosa was heavily infiltrated with tumor, very few endometrial glands remaining. Much melanin was extracellular in the mucosa in coarse and finely granular masses. Tumor cells were found in lymph vessels in the deeper muscle layers. Often the endothelium of such lymphatics was

swollen and had taken up considerable finely granular melanin pigment. A study of individual tumor cells revealed many interesting variations in the intracellular disposition of the pigment. As a whole, the cells were large polyhedral, distinctly epithelial in appearance, with nuclei of almost corresponding shape, vesicular and with a prominent eosinophilic nucleolus. Many cells were in mitosis. In some cells, the pigment was clustered around a cytoplasmic vacuole which was probably lipoid in nature. Other cells were filled with these closely packed vacuoles and only the interstices were occupied by the pigment. Cells in mitosis contained much pigment also, but usually there was a clear zone between the chromatin and the pigment. The pigment in resting cells was frequently clustered around the nucleus. Other cells contained three or four masses of pigment, each nearly as large as the nucleus, and in such cells a large lipoid droplet could be stained diffusely brown. Except in the cells in mitosis, the more pigment contained in the cytoplasm the more chromatic was the nucleus, the latter sometimes approaching pyknosis.

A leiomyoma, a few millimeters in size, had undergone much hyaline degeneration, with some calcification. Lymphatic invasion of the capsule had occurred, but not of the tumor itself.

There was no tumor in the lumen of the Fallopian tube (isthmus), but many dilated lymph vessels of the wall contained much tumor tissue. Tumor cells were present in many dilated lymph channels in the broad ligament and beneath the perineurium of several small nerve trunks.

The intima of the aorta had undergone much thickening and fatty degeneration. Hemorrhage had occurred into this area of fatty change. The vessels of the adventitia showed slight endothelial proliferation and perivascular lymphocytic reaction. A preaortic lymph node was filled with tumor. The afferent lymph vessels and a vein the size of the azygos were occluded by a tumor thrombus.

There was a moderate degree of nephritis secondary to arteriosclerosis of both large and small vessels of the kidneys. The capsule was thickened, and there were a few subcapsular foci of lymphocytes. The epithelium of numerous convoluted tubules was quite stuffed with globoid masses of brown pigment, and in many tubules were hyaline casts stained brown or brownish green. In many of the collecting tubules this intracellular pigment was present in great amount. It did not stain with potassium ferrocyanid and hydrochloric acid, nor with Sudan III; hence it was probably melanin.

In the bone marrow of a rib, there was hyperplasia of the erythrogenic centers. A secondary type of anemia was present. The leukocyte forming centers were not very active. A few megalokaryocytes were seen. Many large spindle cells containing melanin and numbers of pigmented large mononuclear phagocytes, as well as polymorphonuclear leukocytes which had engulfed pigment, were present in great profusion.

OBSERVATIONS MADE BY OTHER PHYSICIANS

Several Southern dermatologists have written the authors of their experience with pigmented tumors in the negro, and the following quotations from their letters are worthy of record:

Dr. Randolph B. Carmichael of Washington, D. C., says:

Concerning pathologic pigmentation and pigmented tumors in colored people, it is very seldom that I see a case of melanotic sarcoma in a negro. I recall

one that showed a lesion at the ankle and I advised operation at the hip, but the operation was done at the knee, subsequently a hip operation was performed, but metastasis had begun and he died. This was in the days before the Roentgen ray and radium.

Dr. Henry Hazen [4] of Washington, D. C., says that he has seen one case, which is reported in the *Southern Medical Journal.*

Dr. James B. Bullitt of Chapel Hill, N. C., says:

Pigmented tumors are rare. . . . Epithelial tumors are less common than in the white. This is especially true of the malignant epithelial growths. Melanomas are in my experience still more rare.

The following is from Dr. H. E. Menage of New Orleans:

I must admit that I have never had any such case in my private or charity practice, and I have seen many negro patients. I have seen a few light mulattoes with pigmented moles and possibly a black mole once in a long time in the blacker type of the race but never melanosis with or without metastasis. Two of my friends, who specialized in genito-urinary diseases who have large clinics for negroes, do not remember seeing such a case.

Dr. Menage furnished short notes of the following cases of malignant melanotic tumors in colored patients, from the records of the New Orleans Charity Hospital:

A. P., a woman, aged 49, one year ago cut a toe, which became infected, amputation being performed. A mass had been present in the inguinal region for eight months. Two months ago the foot was stepped on. It became sore, and a mass developed on the dorsum of the foot. The roentgen ray showed a malignant tumor involving the foot region of the little toe, with destruction of the phalangeals. The pathologic report of the mass in the foot was that it was a melanosarcoma.

L. T., a woman, had a melanotic tumor of the right foot with enlarged inguinal glands. Amputation was performed at the middle third of the foot. The bone substance showed black spots. Necropsy showed metastatic melanoma of the liver, kidney, lungs, foot and inguinal glands.

L. W., a woman, aged 30, two years before was hit on the head with a lump of coal. The wound healed promptly. There was no trouble until four months ago, when it began to pain. Physical examination revealed on the right side of the forehead a hard mass resembling thickened bone. At operation a piece of periosteum the size of half a dollar, together with a mass of dark hard tissue, was removed. The pathologic report was that the condition was melanotic sarcoma. The patient was discharged and apparently not heard from again.

C. L., a woman, aged 23, had a small growth on the dorsal surface of the left foot, not painful, which was removed under local anesthesia. The diagnosis was melanotic sarcoma.

T. W., a youth, aged 18, had had carcinoma of the thumb, which was amputated. Growth occurred in the axilla and shoulder joint. The clinical diagnosis was melanotic sarcoma of the shoulder joint and chest. No pathologic report had been received.

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4. Hazen, Henry H.: Malignant Moles, Southern M. J. **13**:345, 1920.

COMMENT

In our case, the patient's leg was amputated because it was thought to be gangrenous. In support of this diagnosis were (*a*) the falling off of the small toe; (*b*) the diffuse blackening of the skin to a color more intense than that of the rest of the body; (*c*) swelling due to edema of the affected leg (edema with malignant melanoma is said to be more marked in Caucasians [Gaskill [5]]); (*d*) marked generalized arteriosclerosis. Although northern practitioners see little of the colored race in their work, the entire picture was most unusual, and we are skeptical as to whether a Southern physician could have more nearly approximated the correct diagnosis. Following the amputation, the course of the disease was characteristic of malignant melanoma with widespread metastases, with the exception that the stump even though heavily infiltrated with tumor healed almost completely.

How did the tumor originate? A majority of melanomas in white persons arise in pigmented nevi. Our patient gave no positive information concerning this point, but a small cutaneous pigmented growth may quite well have been overlooked. Cases are reported, however, in which no primary nodule or nevus could be found. Again, a primary growth may be exceedingly small. If a mole in the region of the small toe had been present, a dog bite nine years ago and another less definite injury three years previously may have contributed to its malignant metamorphosis. The case would be noteworthy, then, chiefly because it occurred in a negro.

In the absence of a nevus or other benign pigmented tumor as a starting point, how could a malignant melanoma in a negro arise? In the first place, the pigment must be accounted for. Researches by Dyson [6] and Mierowsky [7] have showed that cutaneous melanin probably is derived from specialized cells in the malpighian layer and that pigment in the corium is a secondary deposit. Mertsching [8] concluded that hair pigment separated at the periphery of the nucleus and that skin pigment is formed in a similar way. He was the first to speak of the nuclear origin of melanin. R. Hertwig,[9] in 1904, described the formation of pigment from chromatin in a heliozoan, *Actinosphaerium eichornii,* during the phase of depression. He regarded the pigment as

5. Gaskill, Henry K.: Melanotic Sarcomas Resulting from Irritation of Pigmented Nevi, J. A. M. A. **60**:341 (Feb. 1) 1913.

6. Dyson, William: An Investigation in Cutaneous Pigmentation in Normal and Pathological Conditions, J. Path. & Bacteriol. **15**:298, 1910.

7. Mierowsky, quoted by Dyson.

8. Mertsching: Histologische Studien ueber Keratohyalin und Pigment, Virchows Arch. f. path. Anat. **116**:509, 1889.

9. Hertwig, R., quoted by Dyson.

useless excessive chromatin. Dolley and Guthrie [10] consider the pigment of heart muscle as melanin, a wear and tear pigment, similar to that found in depressed nerve cells.

Chronic irritation in the region of the small toe of the affected leg following repeated injury might have been an important factor in the development of the tumor, whether or not it began in a nevus. The negro having an excessive number of chromatoblasts in his epidermis, these cells might preponderate in an epithelial tumor. If this reasoning is correct, there must be a melanotic tumor which is a carcinoma, favoring the views of Favera, Unna, Marchand and others. However, it is seen even in this case that frequently the cells found loaded with pigment are spindle or polyhedral, differing from those of most epithelial tumors. Nevertheless, the facility with which epithelial cells change to spindle cells has long been a stumbling block in the recognition of a sarcomatous change in the stroma of a carcinoma.

Does extracellular melanin have a stimulative effect on the rate of growth of epithelial or connective tissue cells? The problem is being studied in this laboratory. Arterial obliteration by senile sclerosis sufficient to cause gangrene of the small toe surely would favor cell depression, at least in the environs of the zone of necrosis, and if Dyson's and Hertwig's observations are given the weight they seem to deserve, an excessive local production of melanin would occur. Much fascinating theorizing might be indulged in over the possible origin or origins of melanotic tumors in the negro's skin.

A final point of interest might be discussed briefly. That is the hyperplastic condition of the suprarenal cortex present in our case, and its relation to the pathologic pigmentation. In Addison's disease there is destruction of the suprarenals and subsequent cutaneous melanosis. Alsberg [11] demonstrated in a melanotic tumor of a horse an enzyme capable of forming pigment from certain products of protein decomposition, among them being tyrosin, phenylalanin and tryptophan, substances which are also produced in the cleavage of epinephrin. The melanosis of Addison's disease is thought by some to be due to the fact that through nonfunction of the suprarenals in the formation of epinephrin substances which ordinarily would be synthesized into epinephrin are converted into melanin, possibly through the action of an enzyme present in the skin. All of these observations and speculations merely suggest that the suprarenals are, in some obscure way, concerned in pathologic pigmentation. Hence the cortical hyperplasia

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10. Dolley and Guthrie: The Pigmentation of Heart Muscle, J. Med. Res. **42**:289, 1921.

11. Alsberg, Carl L.: On the Occurrence of Oxidative Ferments in a Melanotic Tumor of the Liver, J. Med. Res. **16**:117, 1907.

and extension may be expressions of an attempt at compensation for some factor or factors which, while present in the suprarenal, were inadequate in stemming the tide of melanin formation.

SUMMARY

1. Melanotic tumors are uncommon in the colored races. Only one case of malignant melanoma in the negro is found in the American literature.

2. A complete study of a fatal case of malignant melanoma of the left leg in an aged negress, with necropsy findings, is presented.

3. Of chief clinical interest was the syndrome which led to the diagnosis of gangrene of the leg and to amputation supposedly for this condition. This consisted of (*a*) marked generalized arteriosclerosis; (*b*) falling off of the small toe; (*c*) diffuse blackening of the skin of the entire leg; (*d*) edematous swelling.

4. The tumor arose in the region of the small toe and invaded diffusely the subcutaneous tissues, blood and lymph channels, the leg as far as the inguinal ligament being uniformly pitch black. Metastasis occurred to the liver, lungs, kidneys, heart, spleen, uterus and retroperitoneal tissues.

5. The anterior tibial artery at the level of the internal malleolus was entirely obliterated by an arteriosclerotic process. Vascular disease in the region of the small toe undoubtedly caused gangrene of the toe.

6. No pigmented nevus or other growth was found as a starting point. The question is raised as to the possibility of chronic irritation and two fairly definite injuries to the small toe, together with local anemia, being responsible for the genesis of the new growth which may have been derived from the chromatoblasts of the negro's epidermis.

7. Hyperplasia with extension of the suprarenal cortex into the capsule and surrounding fat was also present, and in view of various clinical and chemical observations as to the relation of the suprarenals to pigmentation, it is suggested that this cortical response may have been an expression of an attempt at compensation for some factor which, while present in the suprarenal, was inadequate in stemming the tide of melanin formation.

URTICARIA PIGMENTOSA (NODULAR TYPE) WITH A SUMMARY OF THE LITERATURE

REPORT OF A CASE

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Some manifestations of urticaria pigmentosa are rarely seen. In his excellent summary of the literature up to and including 1905, E. Graham Little [1] pointed out that only sixteen cases of urticaria pigmentosa had been reported in America out of a total of 154, while the English literature contained sixty-two cases, the German thirty-nine, and the French twenty-four. He showed that of 138 cases in which the sex was recorded, eighty-six, or 61.7 per cent., occurred in males and fifty-two in females, and that of 142 cases in which the age was given, seventy-nine, or 55 per cent., began at or before the sixth month of age and twenty-two, or 14 per cent., began after puberty (13 years). Also, of 123 cases in which the type of lesion was stated, eighty-three were of the macular, twelve of the nodular and twenty-eight of the mixed type. The disorder proved to be more common in fair skinned than in dark skinned peoples.

Since that time numerous cases have been recorded in America, probably because of its more general recognition, and it is now considered so common, in its usual form, that probably only a fraction of the ordinary macular and maculonodular cases, as it occurs early in life, are on record.

Urticaria pigmentosa was first described by Nettleship [2] in 1869 as "chronic urticaria leaving brown discolorations behind and of two years duration." The name urticaria pigmentosa was given to the condition by Sangster,[3] but the name xanthelasmoidea suggested by Tilbury Fox [4] seems to describe many of the nodular and maculonodular cases better. Darier,[5] who has studied the condition extensively, also considers that xanthoma is its nearest analogue.

The disease occurs generally in three well marked types: (1) that in which the eruption consists entirely of macules, (2) that in which it consists entirely of nodules, and (3) that in which both macules

1. Little, Graham: Contribution on the Study of Urticaria Pigmentosa. Brit. J. Dermat. **17**:355, 1905; **18**:16, 1906.
2. Nettleship: Brit. M. J. **2**:323, 1869.
3. Sangster: Lancet, May 11, 1878.
4. Fox, Tilbury: Allbutt's System of Medicine, London **8**:485, 1899.
5. Darier: Ann. de dermat. et syph. **2**:339, 1905.

and nodules occur. This is emphasized because of the fact that in many instances cases have been reported as consisting partially or entirely of papules. These are here considered as maculonodular and nodular ones, respectively, when the text of the report makes this feasible. Practically none of these is in the English literature. Also, the majority of purely nodular cases are English ones. The nodular lesions sometimes simulate those of xanthoma, and in rare instances maculonodular and nodular eruptions are associated with vesicle and bulla formation.

A diligent search of the literature accomplished by the use of both the "Index Medicus" and the "Surgeon General's Catalogue" has disclosed reports of 152 cases since Little's monograph on the subject in 1905. Many cases have been reported more than once, and there is much of doubt in the diagnosis of some cases; these factors have been taken into consideration. Numerous cases have undoubtedly been seen which were not reported, and some probably have been reported which escaped notice. The description of the lesions is inadequate in some instances, and it is difficult to determine, therefore, whether a given eruption is entirely nodular or maculonodular. Nodular lesions are known to tend to lose their elevation in the course of years, so some of the cases reported as maculonodular when first observed by the physician may have been entirely nodular at the onset of the eruption.

It is not expedient to review the usual symptomatology and pathology, which has been so well summarized by Little,[1] the authors of the current textbooks and others, but it is proposed to bring the literature to date for statistical purposes and reference, a sufficient number of cases now having been recorded to make a future research of this nature unnecessary and first to report a nodular case.

CASE REPORT

At the March meeting of the Chicago Dermatological Society the author by invitation presented a case of nodular urticaria pigmentosa which came under his observation at The Children's Memorial Hospital. It was generally agreed at the time of presentation that from the clinical findings urticaria pigmentosa would hardly be thought of, and that from the history and clinical findings together it would scarcely more than be considered, although apparently all were in accord with the diagnosis after examining the microscopic sections. The chief peculiarities were the "soft mole"-like appearance of the nodules, all soft and only slightly pigmented, and the small number of lesions. Photographs of the lesions are not appended to this article because of their lack of contrast to the surrounding skin.

Fig. 1.—Section of epidermis and greater part of corium showing degree of infiltration and tendency of cells to row and column formation. × 70.

Fig. 2.—Section of the pars reticularis showing the density of the infiltrate about the hair follicles and blood vessels. × 70.

History.—M. T., a girl, 4 years old when first observed, had an eruption which first appeared at the age of about 4 months, all of the lesions with the exception of a recent one of the palm of the right hand appearing within a few days of each other. The mother said that at that time they consisted of red swollen spots which looked like bed-bug bites, but careful searching for several days revealed no bed-bugs. The swellings, which were distinctly red at first, remained so for three or four months, at which time they began to change to light brown ("tan color") which has since persisted. The lesions itched at times and then became more swollen and pinkish. Some of them seemed to the mother to be getting larger. None had disappeared. The child had always been well. The family history was of no special interest.

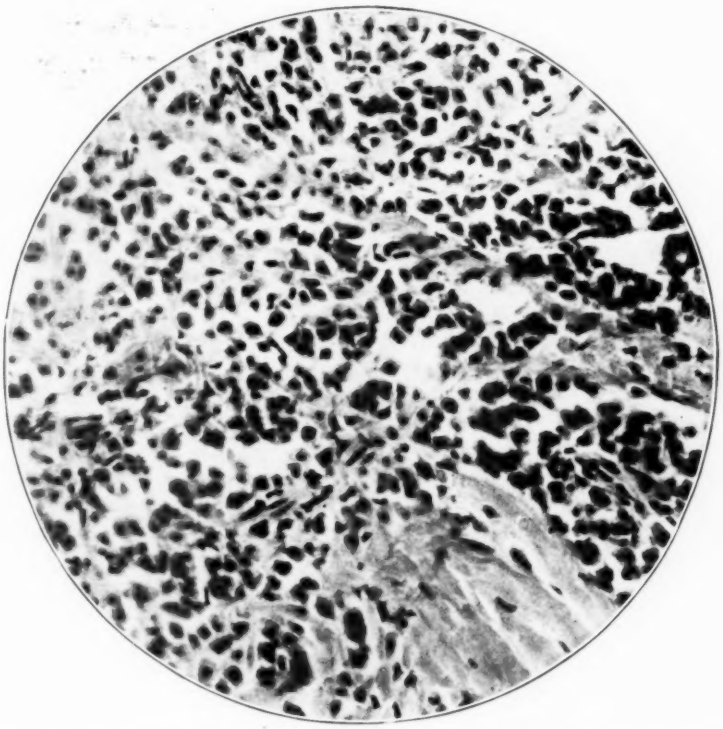

Fig. 3.—Cell infiltration of corium composed almost entirely of cuboidal, oval and fusiform mast cells. × 300.

Examination.—There were sixteen generally distributed lesions, all of which were soft and nodular, some round, some oval, varying in greatest diameter from 0.5 to 2 cm. and with an average elevation of about 3 mm. All were smooth and somewhat resembled large slightly pigmented "moles," with the exception of the two lesions on the left axilla, which were distinctly of nevoid appearance, their surfaces roughened by exaggerated skin lines. These two alone were somewhat suggestive of the lesions of xanthoma. There was no evidence of increased hair growth in any lesion, and all were faintly brownish, the pigment distributed uniformly in some instances and most marked about

the periphery in others. There was one lesion each of the occiput, nucha, epigastrium, right axilla, left labium majorum, right thigh in front, left palm, sacrum and buttock (left and right); and two lesions each of the left axilla, right arm and right thigh (see charts). Urtication could be produced to a marked degree by scratching in two lesions, moderately in four, and slightly or not at all in the others. No lesions could be detected on the buccal mucous membrane. No palpable lymph glands were found enlarged. Dermographism was slight. The patient was fair skinned.

Biopsy.—The right thigh lesion (in which urtication was most marked) was removed for histologic study during the height of that process. The tissue was placed in Zenker's solution and alcohol, blocked in paraffin and stained with Mallory's eosin methylene blue, Giemsa's eosin methylene blue, Pappenheim's methylene green pyronin, hematoxylin eosin, van Gieson's picric acid fuchsin alum hematoxylin, Weigert's connective tissue stain and acid orcein hematoxylin.

There was a dense cellular infiltrate throughout the corium, most pronounced in the lower half, consisting almost uniformly of closely packed mast cells. This determination was made chiefly with Pappenheim's and Giemsa's stains, as no satisfactory polychrome methylene blue was to be had. The granules, which appeared pink in blue cytoplasm with Giemsa's azurated eosin stain and green on a red background with Pappenheim's stain, were much finer than the coarsely granular ones usually seen as representing the Ehrlich type. Some of these were round and oval and some were spindle shaped and branched. These cells were arranged for the most part in columns, each column being separated from the adjacent ones by swollen and torn collagenous bundles. Occasional cells of other varieties were also present (chiefly mononuclear leukocytes and polymorphonuclear cells). The infiltrate was most marked about the hair follicles, blood vessels and sebaceous glands, that in the vicinity of the first mentioned extending sparsely into the subcutaneous tissue. Edema was excessive throughout the corium, and the lymph spaces were widely dilated. Some intercellular edema could be noted in the epidermis. The fibrous bundles throughout the corium were torn into interlacing strands by the edema, clear spaces existing between the fibers.

The papillae and their adjacent rete pegs were decidedly flattened and the interpapillary zone was without cell infiltrate with the exception of a limited number of mast cells about the blood vessels. There was some question as to whether the connective tissue of the corium was increased in amount. Little pigment was demonstrated, and the few granules present were limited to the cells of the germinal layer. There was increased vascularity throughout the corium, most in evidence in the reticular portion.

Elastin was nowhere found with normal arrangement and was most dissociated where the infiltrate was most marked.

Comment.—It does not seem that in this case the degree of pigmentation is in proportion to the degree of mast cell infiltration, as suggested by Little and Raymond (These de Paris, 1888), as the mast cell infiltrate was heavy and the lesions were only slightly pigmented. Hartzell was convinced that in his cases the pigmentation was wholly due to the presence of pigment in the rete and upper part of the corium and not at all to mast cells.

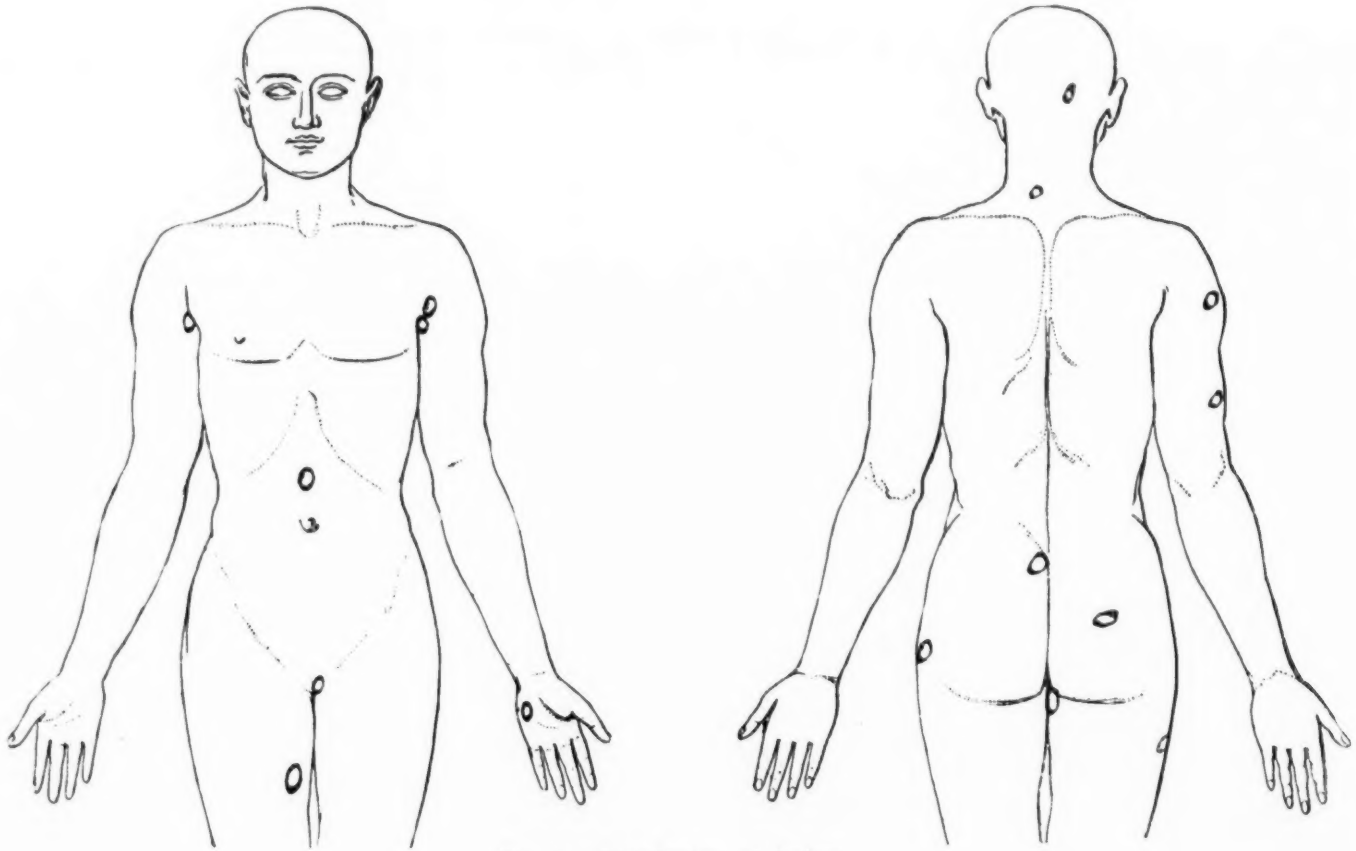

Fig 4. —Distribution of lesions.

CASES REPORTED IN THE LITERATURE

The following two cases of nodular urticaria pigmentosa given by Graham Little [1] are quoted for comparison. These instances illustrate most of the usual similarities and variations.

A boy, aged 1 year, had deep brown walnut-colored nodules raised about one-eighth inch (3.17 mm.) from the surrounding skin and of varying shapes.[6] There were only about thirty lesions in all, one-quarter (6.35 mm.) to one-eighth inch in diameter and situated on the upper arms, thighs, scalp and back. The nodules became swollen and red on irritation. There were no lesions in the mouth. The glands in the back of the neck, axillae and groin were enlarged. There was severe itching. Mast cells were exceedingly copious in the corium and massed about the blood vessels. There were pigmented cells in the basal layer of the epidermis only.

A boy, 4 months old, had an eruption which made its first appearance on the head and face at birth.[7] A fresh outbreak occurred at the age of 1 month, and when the child was first seen at 4 months of age, he had numerous lesions.

The eruption consisted of dark-brown nodules varying in size from one-eighth to 1 inch (2.54 cm.) or more, and raised about one-quarter inch from the surface. The nodules were firm and hard like keloids, with a glistening appearance. They were not itchy. On scratching, the brown color was suffused with pink, and a pink halo surrounded the base of the nodule. The greater part of the eruption was on the back, but lesions were also numerous and large on the scapulae and shoulders. There were a few scattered lesions on the buttocks and back of the thighs, on the legs and arms, and numerous nodules on the face, scalp and neck. The buccal mucous membrane was free. Histologically, pigmented cells were found in the basal layer of the epidermis and in the superimposed layers of the rete. Infiltration of mast cells was found especially to affect the blood vessels of the interpapillary zone, and a general infiltration was also found in the substance of the nodules.

Nodular Cases.—The twelve cases of nodular urticaria pigmentosa quoted by Little were those of Tilbury Fox,[4] in a child 3 months old; Hibblethwaite,[8] in a child of 10 days; Pye-Smith,[9] in a child of 3 years, the disorder being of three months' duration; Crocker,[10] in four cases, in patients aged 8 years, 4 years, 5 weeks and 3 weeks, respectively; Hutchinson,[11] in a youth of 14 years; Little,[1] in two cases, one that of a child at birth and the other at 3 weeks; Morrow,[12] in a child aged 6 months; and Stelwagon,[13] in a child of 3 months.

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6. Footnote 1, p. 364.
7. Footnote 1, p. 370.
8. Hibblethwaite, quoted by Raymond and Little.
9. Pye-Smith, quoted by Raymond and Little.
10. Radcliffe-Crocker: Brit. J. Dermat., 1894, p. 235.
11. Hutchinson: New Sydenham Soc. Atlas, 1903, Part 8, quoted by Little.
12. Morrow, quoted by Raymond and Little.
13. Stelwagon: Jour. cut. dis. **16**:576, 1896.

In the literature since 1905 there were eleven purely nodular cases reported, which, with the one herein recorded, also total twelve. These are the cases of Wallace-Beatty,[14] in a child aged 1 month; Crocker,[15] a child at birth; Jackson,[16] a child of 20 months; Bunch,[17] a child of 2 years; Comby,[18] a child at birth; Stelwagon,[19] a young man at 23 years; Davis,[20] the age of onset not stated; Pernet,[21] a child of 7 months; Heidingsfeld,[22] a young woman aged 18 years; Zeisler,[23] a man of 58 years; and Olson,[24] a woman of 28 years.

In this total of twenty-four recorded nodular cases, by far the majority began in early infancy.

Cases with Xanthoma-Like Lesions.—In this collection of cases, comprising those since 1905, there are ten recorded cases in which there was an eruption consisting entirely or almost so of lesions resembling those of xanthoma. To these has been added a case thoroughly studied by Dr. Ormsby,[25] in 1903, in which a diagnosis was altogether uncertain until after histologic study, a sum total of eleven cases of this type. In the nodular case herein reported, the only lesions which in any way resembled xanthoma were the two of the left axilla. In addition, Fox [26] reported a macular case with lesions altogether of xanthoma color, and Foerster and Baer,[27] reported a macular case with lesions of chamois color and a small lesion of the lobe of the left ear which resembled xanthoma.

The ten cases collected from the literature since 1905, consisting of "xanthoma-like" lesions are those of W. Beatty,[14] in a child of 1 month, with a nodular eruption; the maculonodular case of C. Fox,[28] in a child of 3 months, in whom the lesions began as bullae; Jackson,[16] in a child of 20 months, with a nodular eruption; Lapowski,[29] in a child

14. Beatty, W.: Dublin J. M. Sc. **121**:422, 1906.
15. Crocker: Brit. J. Dermat. **19**:136, 1907.
16. Jackson: J. Cutan. Dis. **26**:418, 1908.
17. Bunch: Brit. J. Dermat. **21**:117, 1909.
18. Comby: Arch. de méd. d'enfants **18**:370, 1915.
19. Stelwagon: J. Cutan. Dis. **33**:216, 1915.
20. Davis: J. Cutan. Dis. **33**:216, 1915.
21. Pernet: Brit. J. Child. Dis. **13**:301, 1916.
22. Heidingsfeld: J. Cutan. Dis. **34**:316, 1916.
23. Zeisler: J. Cutan. Dis. **37**:69, 1919.
24. Olson: Urticaria Pigmentosa, Arch. Dermat. & Syph. **1**:844 (Dec.) 1920.
25. Ormsby: Diseases of the Skin, Philadelphia, Lea & Febriger, 1921, p. 149.
26. Fox, H.: J. Cutan. Dis. **30**:21, 1912.
27. Foerster and Baer: J. Cutan. Dis. **31**:436, 1913.
28. Fox, C.: Brit. J. Dermat. **19**:251, 1907.
29. Lapowski: J. Cutan. Dis. **22**:173, 1909.

with a maculonodular eruption; Fabry,[30] in a maculonodular case which began at birth; Spagenthal,[31] in a similar case beginning at the age of 7 weeks; Trimble and Fordyce, [32] in a 6 months old infant with maculonodular lesions; Comby,[33] in a nodular case noticed at birth and in which vesicles developed on the nodules; Wise,[34] in a 6½-year-old boy with a maculonodular eruption; and Olson,[24] in the 28-year-old woman with the nodular eruption.

It is evident that the onset of this type of the eruption is usually in early infancy. In this instance, as is true in cases of all types in children, mast cells are nearly always found in abundance.

In "adult" or "acquired" cases, mast cells are frequently lacking. Such cases have been reported by Ormsby,[25] Lieberthal,[35] H. Fox,[36] Wise,[37] W. Beatty,[38] and Ormsby and Mitchell,[39] among others. These cases are usually wholly macular and with but mild or even absent urticarial symptoms.

On involution, especially of nodular lesions, scarring has been reported. Hallopeau, Crocker, Wallace-Beatty, Galloway, Brongersma and others cite such instances.

In eight cases since 1905, vesicobullous lesions were noted. Cyclic bullous lesions appeared in the maculonodular case of Hallopeau and Tessiere,[40] in a boy of 10 years, making the diagnosis somewhat uncertain. The maculonodular case of Macleod [41] in a child of 4 months began as a partially bullous eruption, as was the instance in C. Fox's [28] case and the nodular case of Crocker.[15] In G. H. Fox's [42] case, consisting of a macular eruption, bullous lesions were associated, and in the maculonodular case of Nicolas and Moutot [43] some papulovesicular lesions were noticed. Vesicles developed on the nodules in the cases

30. Fabry: Arch. f. Dermat. u. Syph. **113**:269, 1912.
31. Spagenthal: Buffalo M. J. **69**:76, 1913-1914.
32. Trimble and Fordyce: J. Cutan. Dis. **32**:151, 1914.
33. Comby: Arch. de méd. d'enfants **18**:370, 1915.
34. Wise: Urticaria Pigmentosa, Arch. f. Dermat. u. Syph. **1**:223 (Feb.) 1920.
35. Lieberthal: J. Cutan. Dis. **36**:243, 1918.
36. Fox, H.: Urticaria Pigmentosa, Arch. Dermat. & Syph. **4**:407 (Sept.) 1921.
37. Wise: Urticaria Pigmentosa, Arch. Dermat. & Syph. **3**:325 (March) 1921.
38. Beatty, W.: Brit. J. Dermat. **33**:151, 1921.
39. Ormsby and Mitchell: Urticaria Pigmentosa, Arch. Dermat. & Syph. **7**:134 (Jan.) 1923.
40. Hallopeau and Tessiere: Bull. Soc. franç. de dermat. et syph. **16**:84, 1905.
41. Macleod: Brit. J. Dermat. **19**:75, 1907.
42. Fox, G. H.: J. Cutan. Dis. **28**:676, 1910.
43. Nicholas and Moutot: Lyon méd. **113**:1088, 1909.

of Comby [33] and Pusey [44] and were present in Macleod's [45] 3-month-old child with a maculonodular eruption. Dr. Pusey's case was unique in that in no other did such lesions occur in the "acquired" type.

In the following appendix is included a résumé of the recorded cases since Graham Little's report.

APPENDIX

Reporter	Reference	Sex	Age at Onset	Type	Remarks
Vershiniu	Med. Oboz. Mosk. **62**: 463, 1904	.....	.....	.....	Not available
Toyama	Hifubyog Kiu Hinioch Tokyo **6**: 6, 1905	.....	.....	.....	Not available
MacMaster	Austral. Med. Gas. **24**: 270, 1905	Male	3 months	Macular	
Gassmann	Dermat. Ztschr. **12**: 284, 1905	Male	37 years	Macular	
Hallopeau and Tessiere	Bull. Soc. franç. de dermat. et syph. **16**: 84, 1905	Male	10 years	Maculo-nodular	Questionable case and associated with cyclic bullous lesions
Lieberthal	Illinois M. J. **8**: 432, 1905	Female	6 weeks	Macular	
Bohac	Arch. f. Dermat. u. Syph. **82**: 49, 1906	Female	27 years	Macular	
Mewborn	J. Cutan. Dis. **24**: 331, 1906	Male	36 years	Macular	
Beatty, W.	Dublin. J. M. Sc. **121**: 422, 1906	Male	1 month	Nodular	Xanthoma-like lesions
Engel	Arch. f. Kinderh. **43**: 156, 1906	Male	8 days	Maculo-nodular	
Vörner	Dermat. Ztschr. **13**: 274, 1906	Female	37 years	Macular	
Stainer	Brit. J. Dermat. **18**: 186, 1906	Not stated	6 months	Macular	
Macleod	Ibid. **19**: 75, 1907	Female	4 months	Maculo-nodular	Began as partially bullous eruption
Crocker	Ibid., 136	Female	Birth	Nodular	Began as bullae
Morris	Ibid., p. 205	Not stated	3 months	Macular	
Morris	Ibid.	Not stated	2 years	Macular	
Fox, C.	Ibid., p. 251	Male	3 months	Maculo-nodular	Xanthoma-like lesions; began as bullae
Van der Hoof	Nederl. Tijds. f. Geneesk. **1**: 515, 1907	.....	.....	.....	Not available
Swoboda	Mitt. Gesell. f. inn. Med. **6**: 73, 1907	.....	.....	.....	Not available
Jacob	Brit. M. J. **1**: 1301, 1907	Male	13 months	Maculo-nodular	Treated by roentgen rays, cleared and recurred
Adamson	Proc. Roy. Soc. Med., Dermat. Sec. **1**: 63, 1907-1908	Male	2 years	Macular	
Little	Ibid., p. 165	Female	32 years	Macular	
Klotz	Arch. f. Dermat. u. Syph. **87**: 231, 1907	Female	1½ years	Maculo-nodular	Under title of xanthelasmoidea naeviformis
Bonnet	Lyon méd., 1908, p. 1164	Male	10 months	Macular	
Hutchinson	Scott. M. & S. J. **22**: 493, 1908	Male	"Child"	Macular	
Adamson	Brit. J. Dermat. **20**: 127, 1908	Male	2 years	Macular	
Little	Ibid., p. 232	Female	32 years	Macular	
Kanitz	Pest. med.-chir. Presse **44**: 1073, 1908	.....	.....	.....	Not available
Bowen	J. Cutan. Dis. **26**: 177, 1908	Female	"Shortly after birth"	Macular	
Jackson	Ibid., p. 418	Female	20 months	Nodular	Xanthoma-like lesions

44. Pusey, W. A.: J. Cutan. Dis. **35**:48, 1917.

45. Macleod: Proc. Roy. Soc. Med. **14**:17, 1920.

APPENDIX—*Continued*

Reporter	Reference	Sex	Age at Onset	Type	Remarks
Saville.....	Hospital, Lond. **43**: 541 1908	.....	.....	.....	Not available
Rother.....	Monog., Leipzig, 1908.....	.....	Adult	.....	Nothing more available
Bunch.....	Brit. J. Dermat. **21**: 117, 1909	.....	2 years	Nodular	
Bunch.....	Ibid., p. 219.....	Female	9¾ years	Macular	
Meachen.....	Ibid., p. 349.....	Male	3½ months	Macular	
Lapowski.....	J. Cutan. Dis. **22**: 173, 1909	Male	"Child"	Maculo-nodular	Xanthoma-like lesions
Schwartz.....	Ibid., p. 206.....	Not stated	3 months	Macular	
Pautrier and Fernet	Bull. Soc. Franç. de dermat. et syph. **20**: 107, 1909	Male	19 years	Maculo-nodular	
Ercoli.....	Gior. ital. d. mal. ven. **44**: 354, 1909	Male	20 years	Maculo-nodular	
Pelagatti.....	Ibid., p. 534.....	Female	58 years	Maculo-nodular	
Nicolas and Moutot	Lyon méd. **113**: 1088, 1909	Female	Birth	Maculo-nodular	Some papulovesicular lesions
Little.....	Proc. Roy. Soc. Med., Dermat. Sec. **3**: 3, 1910	Not stated	2 weeks	Maculo-nodular	
Montagnon....	Loire méd. **29**: 409, 1910..	.....	.....	.....	Not available
Kanitz.....	Pest. med.-chir. Presse **46**: 118, 1910	.....	.....	.....	Not available
Fox, G. H.	J. Cutan. Dis. **28**: 676, 1910	Female	2 months	Macular	Some bullous lesions
Hyde.....	Ibid., p. 480.....	Female	1 year	Maculo-nodular	
Bizzozero.....	Ann. de dermat. et syph. **2**: 385, 1911	Male	3 months	Macular	
Gottheil.....	J. Cutan. Dis. **29**: 242, 1911	Female	10 days	Macular	
Fox, G. H.	Ibid., p. 495.....	Male	43 years	Macular	Questionable case
Little.....	Brit. J. Dermat. **23**: 184, 1911	Male	8 months	Macular	
Bunch.....	Ibid., p. 405.....	Not stated	2 months	Macular	
Rott.....	Berlin klin. Wchnschr. **48**: 86, 1911	Female	3 weeks	Macular	
Little.....	Proc. Roy. Soc. Med., Dermat. Sec. **4**: 103, 1911	Male	7 weeks	Macular	
Little.....	Ibid., p. 104.....	Female	22 years	Macular	
Fox, H.	J. Cutan. Dis. **30**: 21, 1912	Female	3 months	Macular	But of color of xanthoma
Hartzell.....	Ibid., p. 491.....	Female	2 weeks	Macular	Pigmented areas were large
Lancashire.....	Brit. J. Dermat. **24**: 320, 1912	Male	Birth	Macular	
Biach.....	Arch. f. Dermat. u. Syph. Orig. **111**: 619, 1912	Male	6 years	Macular	
Biach.....	Ibid	Female	36 years	Macular	
Fabry.....	Ibid. **113**: 269, 1912	Male	Birth	Maculo-nodular	Xanthoma type
Dubreuilh.....	Ann. de dermat. et syph. **3**: 494, 1912	Female	3 months	Maculo-nodular	
Rasch.....	Hospitalstidende, 5R.**5**: 1569, 1912	Male	6 months	Maculo-nodular	
Boas.....	Ibid., p. 905.....	Male	6 months	Maculo-nodular	
Gavini.....	Bull. d. sc. med., Bologna p. 517, 1913	Female	14 years	Macular	
Heller.....	Dermat. Ztschr. **20**: 806, 1913	Not stated	Birth	Maculo-nodular	
Spagenthal....	Buffalo M. J. **69**: 76, 1913-1914	Female	7 weeks	Maculo-nodular	"Similar to xanthoma"
Kerl.....	Arch. f. Dermat. u. Syph. **118**: 563, 1913	Female	2 months	Maculo-nodular	
Kerl.....	Ibid.	Male	13 years	Maculo-nodular	
Riehl.....	Wien. med. Wchnschr. **63**: 2565, 1913	Male	10 days	Macular	
Hartzell.....	J. Cutan. Dis. **31**: 117, 1913	Female	2 weeks	Macular	
Foerster and Baer	Ibid., p. 436.....	Male	2 months	Macular	"Chamois color; small lesion of lobe of ear resembling xanthoma"
Jeanselme and Touraine	Bull. Soc. franç. de dermat. et syph. **24**: 426, 1913	Female	Birth	Macular	

APPENDIX—*Continued*

Reporter	Reference	Sex	Age at Onset	Type	Remarks
Adamson.....	Proc. Roy. Soc. Med., Dermat. Sec. **7**: 104, 1913-1914	Female	39 years	Macular	
Meachen.....	Brit. J. Dermat. **25**: 140, 1913	Male	2 years	Macular	
Semon.....	Ibid., p. 265.....	Not stated	6 months	Macular	
Heath.....	Ibid., p. 410.....	Male	"Young man"	Macular	
Brotman.....	Russk. Zhurnal, 1914, p. 305	Not stated	1 month	Macular	
Jadassohn.....	Cor.-Bl. f. schweiz. Aerzte **44**: 1479, 1914	Female	15 years	Macular	
Trimble and Fordyce	J. Cutan. Dis. **32**: 151, 1914	Male	6 months	Maculo-nodular	"Some lesions looked very much like xanthoma"
Becht.....	Ibid., p. 511.....	Male	3 years	Macular	
Adler.....	Dermat. Ztschr. **21**: 761, 1914	Male	Birth	Macular	
Hoffmann.....	Berlin klin. Wchnschr. **40**: 962, 1914	Male	Birth	Maculo-nodular	
Comby.....	Arch. de méd. d. enf. **18**: 370, 1915	Male	Birth	Nodular (vesicles develop on nodules)	Xanthoma type; also reports 3 cases of urticaria with pigmentation
Knowles.....	J. Cutan. Dis. **33**: 171, 1915	Male	3 months	Macular	
Knowles.....	Ibid.	Female	3 months	Macular	
Knowles.....	Ibid.	Female	4 years	Macular	
Knowles.....	Ibid.	Female	6 years	Macular	
Knowles.....	Ibid.	Female	10 years	Macular	
Stelwagon.....	Ibid., p. 216.....	Male	23 years	Nodular	
Davis.....	Ibid., p. 216.....	Not stated	.....	Nodular	
Shaffner.....	Ibid., p. 397.....	Not stated	Birth	Macular	
Whitehouse....	Ibid., p. 855.....	Male	4½ years	Macular	
Fordyce.....	Ibid., p. 857.....	Male	3 months	Maculo-nodular	"Slightly elevated papules"
Dore.....	Proc. Roy. Soc. Med., Dermat. Sec. **8**: 11, 1915	Male	23 years	Macular	
Pernet.....	Ibid., p. 157.....	Male	Birth	Macular	
Little.....	Ibid., p. 216.....	Male	17 years	Macular	
Bang.....	Ugesk. f. Læger **78**: 1740, 1916	Male	5 months	Macular	
Sibley.....	Brit. J. Dermat. **28**: 327, 1916	Male	19 years	Macular	
Cassar.....	Ann. de dermat. et syph. **6**: 95, 1916	Male	15½ years	Maculo-nodular	
Pernet.....	Brit. J. Child. Dis. **13**: 301, 1916	Male	7 months	Nodular	
Shelmire... ...	Texas State J. M. **12**: 267, 1916	Female	16 months	Macular	
Tieche.....	Cor.-Bl. f. schweiz. Aerzte **46**: 1494, 1916	Male	16 years	Macular	
Fordyce.....	J. Cutan. Dis. **34**: 120, 1916	Female	Birth	Maculo-nodular	
Trimble.....	Ibid., p. 405.....	Male	1 year	Macular	
Kingsbury.....	Ibid., p. 558.....	Not stated	4 months	Macular	
Stillians	Ibid., p. 615.....	Female	3 months	Maculo-nodular	
Bechet.....	Ibid., p. 685.....	Not stated	4 months	Maculo-nodular	
Whitehouse....	Ibid., p. 767.....	Female	3 years	Macular	Sisters; "some of the lesions suggested nevi"
Whitehouse....	Ibid.	Female	13 years	Macular	
Clark.....	Ibid., p. 767.....	Male	6 years	Macular	
Pusey.....	Ibid. **35**: 48, 1917.....	Male	22 years	Maculo-nodular	Vesicles on nodules
Fordyce.....	Ibid., p. 543.....	Not stated	22 months	Maculo-nodular	
Hartzell.....	Ibid., p. 756.....	Male	23 years	Maculo-nodular	
Ormsby.....	Ibid., p. 855.....	Female	27 years	Maculo-nodular	Mast cells were not present
Hartzell.....	Ibid. **36**: 184, 1918.....	Female	19 years	Macular	
Goldenberg....	Ibid. **36**: 188, 1918.....	Female	15 years	Macular	
Lieberthal.....	Ibid., p. 243.....	Female	28 years	Not stated	No mast cells
Heidingsfeld...	Ibid., p. 316.....	Female	18 years	Nodular	
Mackey.....	Ibid., p. 320.....	Female	Birth	Macular	

APPENDIX—*Continued*

Reporter	Reference	Sex	Age at Onset	Type	Remarks
Ormsby.....	Ibid., p. 469.....	Female	Birth	Macular	
Bunch.....	Proc. Roy. Soc. Med., Dermat. Sec. **12**: 1, 1918-1919	Male	6 years	Macular	
Montpellier....	Ann. **7**: 32, 1918-1919.....	Male	Birth	Maculo-nodular	
Jeanselme and Touraine	Bull. Soc. franç. de dermat. et syph. 1919, p. 98	Male	15 years	Maculo-nodular	
Zeisler.....	J. Cutan. Dis. **37**: 69, 1919	Male	58 years	Nodular	
Wise.....	Ibid., p. 132.....	Male	42 years	Macular	
Ormsby and Mitchell	Ibid., p. 269.....	Female	21 years	Maculo-nodular	
Wise.....	Ibid., p. 360.....	Female	4 months	Maculo-nodular	
Harris.....	Ibid., p. 541.....	Male	27 years	Maculo-nodular	
Harris.....	Ibid., p. 625.....	Not stated	Birth	Macular	Questionable case
Thibierge.....	Bull. Soc. franç. de dermat. et syph. **27**: 9, 1920	Female	7 months	Macular	
Macleod.....	Proc. Roy. Soc. Med. Dermat. Sec. **14**: 17, 1920	Not stated	3 months	Maculo-nodular	Associated with vesicles and bullae
Wise.....	Arch. Dermat. & Syph. **1**: 223 (Feb.) 1920	Male	6½ years	Maculo-nodular	Xanthoma-like lesions (?)
Oliver.....	Ibid. **2**: 112 (July) 1920..	Female	34 years	Macular	
Fordyce.....	Ibid. **2**: 264 (Aug.) 1920..	Male	27 years	Macular	
Wise.....	Ibid. **3**: 325 (March) 1921	Male	40 years	Maculo-nodular	Found no mast cells
Abramovitz....	Ibid., p. 331.....	Not stated	1 month	Macular	
Clark.....	Ibid. **3**: 869 (June) 1921...	Female	18 years	Maculo-nodular	
Fox, H.	Ibid. **4**: 407 (Sept.) 1921..	Female	27 years	Macular	No mast cells
Olson.....	Ibid. **4**: 844 (Dec.) 1921...	Female	28 years	Nodular	Resembling xanthoma mast cells = +++
Beatty, W.	Brit. J. Dermat. **33**: 151, 1921	Male	22 years	Maculo-nodular	
Bunch.....	Ibid., p. 28.....	Not stated	9 months	Maculo-nodular	
Eliascheff.....	Bull. Soc. franç. de dermat. et syph. **28**: 17, 1921	Female Male	34 years 15 years	Macular Macular	Mast cells found
Mandel.....	Ibid., p. 52.....	Female	38 years	Macular	
Milian and Perin	Ibid., p. 126.....				
Margarot and Bourgoing	Bull. Soc. d. sc. méd. et biol. de Montpellier **3**: 488, 1921	Female	18 years	Macular	
Rostenberg....	Arch. Derm. & Syph. **5**: 400 (March) 1922	Female	9 weeks	Macular	
Covisa.....	Ibid. **5**: 522 (April) 1922..	Not stated	8 months	Macular	
Gager.....	Ibid. **6**: 123 (July) 1922..	Male	19 years	Macular	
Michelson.....	Ibid. **6**: 644 (Nov.) 1922..	Not stated	6 weeks	Macular	
Parounagian..	Ibid. **7**: 123 (Jan.) 1923..	Male	31 years	Maculo-nodular	
Ormsby and Mitchell	Ibid. **7**: 134 (Jan.) 1923..	Male	49 years	Macular	No mast cells
Crawford.....	Ibid. **7**: 563 (April) 1923..	Female	12 years	Macular	

SUMMARY

Summary of the Collected Cases Since 1905.—Total: Since 1905, a total of 152 cases of urticaria pigmentosa have been reported. Particulars were not obtainable in nine cases.

Sex: Of 122 cases in which the sex was stated, sixty-five, or 53.3 per cent., were males and fifty-seven, or 46.7 per cent., were females.

Age at Onset: Of 143 cases in which the age at onset was given, sixteen, or 11 per cent., began at birth; fifty-nine, or 41.2 per cent., began at or before the sixth month of age; sixty-six, or 46.1 per cent., began within the first year; ninety-six, or 67.1 per cent., began before puberty (13 years); and forty-seven, or 32.9 per cent., were "adult" cases.

Type of Lesion: Of 141 cases in which the type of lesion was stated or could be determined fairly accurately, eighty-seven, or 61.7 per cent., were macular; eleven, or 7.8 per cent., were nodular; and forty-three, or 30.5 per cent., were maculonodular. Of these, and in addition the case included in Reference 25, eleven, or 7.7 per cent., consisted of "xanthoma-like" lesions, and eight, or 5.5 per cent., were associated with vesicle and bulla formation.

Comparison: In comparison to Little's figures, in which approximately the same number of cases were considered, notable differences are present in the incidents of frequency as regards sex, age at onset and type of lesions. He found that about 62 per cent. of the cases were in males in comparison to this figure of about 53 per cent.

In 55 per cent of his cases, the eruption appeared before or during the sixth month of age, in comparison to this percentage of 41. Of cases recorded up to 1905, only 14 per cent. began in adult life (after 13 years of age), in striking contrast to this recent total of 32 per cent. as "adult" cases.

This probably is due to the more general recognition of "acquired" urticaria pigmentosa and to the fact that many ordinary "congenital" cases unquestionably escape report.

In Little's report, 67 per cent. of the cases were of macular type, as compared to about 62 per cent. since then; nearly 10 per cent. were nodular as compared to 7.8 per cent.; and 22 per cent were maculonodular as compared to the recent group, which totals 30.5 per cent.

Summary of All Cases of Urticaria Pigmentosa Reported to Date.—A sum total of 308 cases of urticaria pigmentosa have been collected, including the case mentioned in Reference 25 with xanthoma-like lesions and the nodular case herein reported, a number great enough to offer fairly accurate statistics and to make further summarization of this nature unnecessary.

Sex: Of 262 cases in which the sex was stated, 152, or 58 per cent., occurred in males.

Age at Onset: Of 286 cases in which the age at onset was given, 139, or 48.6 per cent., began before or at the sixth month of age and sixty-nine, or 24 per cent., began after puberty, the so-called "acquired" or "adult" cases. (This figure probably is a little high for reasons above mentioned.)

Type of Lesions: Of 266 cases in which the type of lesion was stated, 170, or approximately 64 per cent., were of the macular, twenty-five, or 9.4 per cent., of the nodular, and seventy-one, or 26 per cent., of the maculonodular.

As mentioned, in the 141 collected cases since 1905 in which the type of lesion was stated, eight, or 5.5 per cent., were associated with vesicle and bulla formation. In this group of cases, and in addition the case mentioned in Reference 25, eleven, or 7.7 per cent., were of the "xanthoma type."

Of the total collected cases, ninety-eight are in the English literature, eighty-three in the American, fifty-seven in the German and forty-one in the French.

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BIOLOGIC REACTIONS OF ARSPHENAMIN

VII. THE RELATIVE THERAPEUTIC EFFICIENCY OF GELATIN ARSPHENAMIN AND DISODIUM ARSPHENAMIN *

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In the preceding article, we have shown that the compound formed of gelatin and arsphenamin is considerably less toxic than is arsphenamin alone. The chemical toxicity of this compound was three-fifths of that of the original arsphenamin from which it was prepared, its physical toxicity was completely removed, and the circulatory disturbances which follow the administration of arsphenamin were reduced or under certain conditions entirely prevented.[1] It was further shown that the basic factor in the production of these results was the binding of the arsphenamin by the gelatin rather than by the body cells and fluids. The question has arisen whether its action on the organisms for whose destruction the drug is intended is not also lessened. The present study is an investigation of this point.

Two factors at least will influence the efficiency of a parasiticidal drug when it is administered in vivo; first, the degree of its specific action on the parasites concerned; and second, the concentration of it which is maintained in the animal's blood stream and tissues after its administration. This latter factor is largely dependent on the rate of excretion of the drug, for Voegtlin [2] has shown with different arsenicals that the more rapid their excretion, the less is their therapeutic activity. Both these factors in the case of gelatin arsphenamin are unknown. *A priori,* it seems likely that arsphenamin bound by gelatin would be less active in the destruction of parasites than free arsphenamin; yet, on the other hand, such a complex as gelatin arsphenamin is less diffusible and therefore is probably less readily excreted than free arsphenamin. Both these points were experimentally determined before proceeding to the actual comparison of the therapeutic effect of the two forms.

There are several experimental methods available for the testing of drugs designed for the treatment of syphilis. Ehrlich and Hata [3] used

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1. Oliver, J., Yamada, S. S., and Kolos, F.: Biologic Reactions of Arsphenamin. VI. The Reduction of Its Toxicity by Combination with Hydrophil Colloids, Arch. Dermat. & Syph. **8**:1 (July) 1923.

2. Voegtlin, C., and Thompson, J. W.: J. Pharmacol. & Exper. Therap. **20**:85, 1922.

3. Ehrlich, P., and Hata, S.: Die experimentelle Chemotherapie der Spirillosen, Berlin, J. Springer, 1910.

for this purpose spirillosis of fowls, *Spironema* of relapsing fever inoculated into mice, and rabbit syphilis. Castelli [4] compared the efficiency of arsphenamin and neo-arsphenamin by the same technic. Recently, however, experimental trypanosomiasis has largely replaced all other methods, for not only are the ends results sharply defined, but comparative experiments have shown that these results are directly comparable to those obtained with the same drugs in the treatment of human syphilis (Dale and White [5]).

Schamberg, Kolmer and Raiziss [6] have compared the efficiency of arsphenamin and neo-arsphenamin by such tests. Their method is briefly as follows: Rats of from 100 to 150 gm. in weight are inoculated with from 250,000 to 500,000 of *Trypanosoma equiperdum* intraperitoneally. The parasites are counted in a special diluting fluid with a blood counting pipet and chamber. Twenty-four hours later, the drug is injected intravenously. Blood from the tail of the animal is now examined for parasites every day for a period of twenty-one days. Untreated controls are run with each experiment, and these regularly develop a blood stream infection on the third or fourth day following the inoculation. The "therapeutic dose" is taken as that one which prevents the development of the infection.

Voegtlin [7] in a comparison of neo-arsphenamin and arsphenamin, has somewhat modified this procedure. Rats of from 100 to 150 gm. in weight are inoculated intraperitoneally with *T. equiperdum*. As soon as the animals show the presence in their blood stream of approximately 100,000 trypanosomas per cubic millimeter, a point determined by counts made with Kolmer's technic on blood from the tail, the drug is injected intravenously. The blood is then examined on successive days. As an end point, Voegtlin takes the minimum effective dose, that is, the amount which clears the blood stream of parasites in twenty-four hours. Relapses occur, but these are not considered.

In our experiments, we have followed Voegtlin's method. It has the advantage of treating an established infection of constant severity. We did, however, take into account the occurrences of relapses.

Experimental

The Trypanocidal Activity of Arsphenamin and Gelatin Arsphenamin

An emulsion of *Trypanosoma brucei* in 0.9 per cent. sodium chlorid solution was prepared by differential centrifugalization of the oxalated

4. Castelli, G.: Ztschr. f. Chemotherap., Orig. **1**:321, 1912.

5. Dale, H. H., and White, C. F.: The Lancet, **202**:779, 1922.

6. Schamberg, J. F.; Kolmer, J. A., and Raiziss, G. W.: Am. J. M. Sc. **160**:25, 1920.

7. Voegtlin, C., and Miller, D. W.: Public Health Repts. **37**:1627, 1922.

blood of a heavily infected rat. In this way, a solution containing only an occasional blood cell and a large number of trypanosomes was secured. Five-tenths cubic centimeter of this suspension was placed in each of two series of small tubes, and there was then added to one series 0.5 c.c. of increasing dilutions of disodium arsphenamin, and to the other series, an equal amount of gelatin arsphenamin. A control tube contained 0.5 c.c. of 0.9 per cent. sodium chlorid and 0.5 c.c. of the trypanosome suspension. The tubes were agitated and kept at room temperature. At frequent intervals, ranging from one to five minutes, a drop of the mixture was removed from each tube, examined microscopically with the high dry objective and the time noted at which all the trypanosomes were killed. Table 1 gives the results of a typical experiment.

It will be seen that the rate of trypanocidal action of gelatin arsphenamin is somewhat slower in vitro than that of disodium arsphenamin, but at the highest dilution tested, 1 : 204,800, it was still definitely active.

TABLE 1.—*Death Point of Trypanosomes in Vitro* *

	Concentration of Drug						
	1:6,400	1:12,800	1:25,600	1:51,200	1:102,400	1:204,800	Control†
Disodium arsphenamin	.....	5 min.	12 min.	20 min.	45 min.	70 min.	¶
Gelatin arsphenamin...	7 min.	17 min.	28 min.	51 min.	67 min.	110 min.	¶

* 0.5 c.c. trypanosome suspension + 0.5 c.c. drug dilution.
† indicates 0.5 c.c. trypanosome suspension + 0.5 c.c. 0.09 sodium chlorid.
¶ indicates no dead trypanosomes found at the end of 120 minutes.

THE EXCRETION OF DISODIUM ARSPHENAMIN AND GELATIN ARSPHENAMIN

The usual method of determining the degree of excretion of arsphenamin has been the estimation of it in the urine and feces. It is known that the greater part is eliminated by the bowel, and since it is difficult to collect these specimens with regularity from animals, the results of such experiments are often unsatisfactory. A more accurate result may be obtained by the converse experiment, in which is determined the amount of arsphenamin which has been retained in the animals' tissues and blood after a certain period. This was the method used by Voegtlin,[2] and which we have adopted. The procedure was as follows: Five small rats, weighing 50 gm., were given intravenously 0.02 gm. per kilogram of disodium arsphenamin, or of gelatin arsphenamin, in 0.5 per cent. solution. The animals were then killed twenty-four, forty-eight, seventy-two and ninety-six hours later. The abdominal cavity was opened, care being taken to lose no blood, the bladder emptied of urine and the gastro-intestinal tract washed free from its contents. All of the tissues of the animal were now finely minced, and the

organic material destroyed with concentrated sulphuric acid and nitric acid in the usual way. The arsenic was determined in aliquot portions by the Gutzeit method. The method was repeatedly checked by determining the arsenic in an animal killed immediately following the injection of a similar dose of arsphenamin, whose excretions were not removed. Thirty-two experiments were performed, not counting the control determinations. The amounts of arsenic retained are shown in Table 2 in the form of percentages of the amount of arsenic injected.

There is a larger amount of gelatin arsphenamin retained by the animal than is the case with disodium arsphenamin.

This finding is supplemented by four experiments in which the arsenic excreted in the urine was determined with rabbits. Although the number of experiments is small, the results are so consistent and conclusive that they are presented here.

TABLE 2.—*Percentage of Arsenic Retained After Injection of Disodium Arsphenamin and Gelatin Arsphenamin*

	24 Hours		48 Hours		72 Hours		96 Hours	
Experiment No.	Arsphenamin	Gelatin arsphenamin	Arsphenamin	Gelatin arsphenamin	Arsphenamin	Gelatin arsphenamin	Arsphenamin	Gelatin arsphenamin
1.....	37	50	16	30	7	25	3	10
2.....	29	40	12	12	5	12	9	15
3.....	35	40	17	28	15	28	11	15
4.....	28	57	13	24	15	22	18	16
Average.....	32	47	14	23	10	21	10	14
Ratio.....	1	1.5	1	1.6	1	2.1	1	1.4

Four rabbits were given 0.015 and 0.03 gm. per kilogram of disodium arsphenamin and of gelatin arsphenamin per kilogram. The animals were catheterized immediately before the injection and the urine collected in twenty-four hour periods by catheterization. The arsenic content of the urine is shown in Figure 1 as percentages of the total amount of arsenic injected.

It is seen that there is a marked difference in the first two days of the experiment, the excretion of the arsenic from the animal which had received disodium arsphenamin being 100 per cent. greater during that period than the amount excreted by the animal which was given gelatin arsphenamin. After this period, the excretion of the two preparations by the kidney was practically equal.

Of the two factors on which the therapeutic efficiency of the drug depends, trypanocidal activity and retention in the body of the treated animal, the former is found to a greater degree with disodium arsphenamin, and the latter with gelatin arsphenamin. These relations are shown in Figure 2.

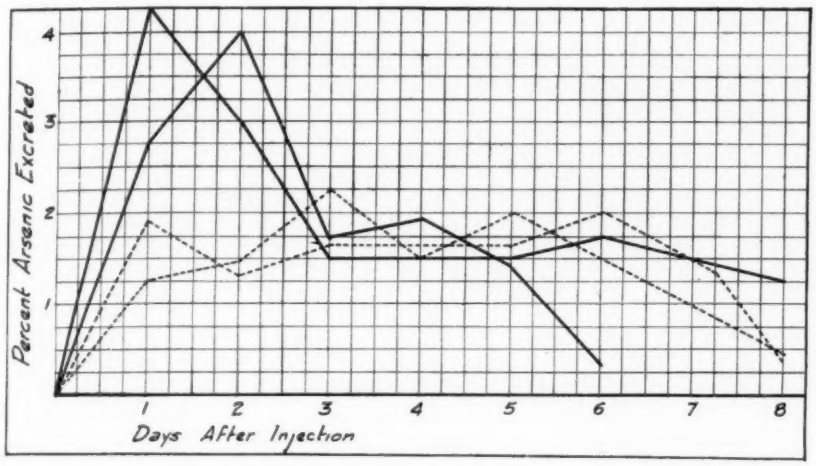

Fig. 1.—Excretion of arsenic in urine after injection of disodium arsphenamin and gelatin arsphenamin. The continuous line indicates disodium arsphenamin, the broken line, gelatin arsphenamin.

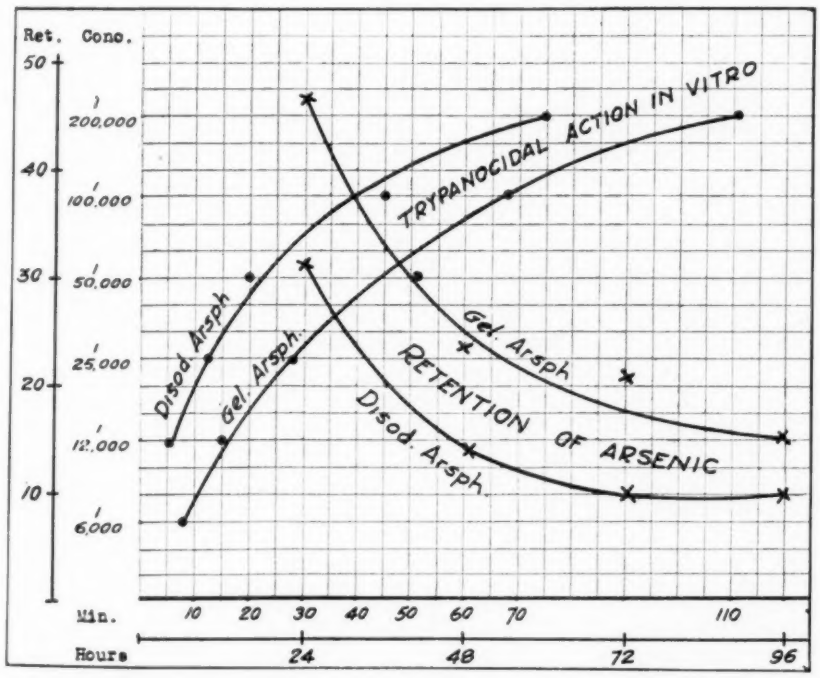

Fig. 2.—Retained arsenic and concentrated arsenic in vitro with disodium arsphenamin and with gelatin arsphenamin. The first column of figures to the left of the chart indicates the percentage of arsenic retained; the second column, concentration of arsenic in vitro.

It must be remembered in considering this graph that the two sets of curves are not directly comparable, as the abscissas and ordinates represent different values. But it does represent the essential fact that though gelatin arsphenamin is not quite as active in its trypanocidal action as disodium arsphenamin, when it is injected into an animal a higher concentration of it is maintained for a longer time than is the case with the latter form of the drug. Whether this latter factor will raise its efficiency in vivo to, or above, that of disodium arsphenamin must be determined by direct experiment.

THE THERAPEUTIC EFFICIENCY OF DISODIUM ARSPHENAMIN AND GELATIN ARSPHENAMIN IN EXPERIMENTAL TRYPANOSOMIASIS

In these experiments, rats were inoculated intraperitoneally with *Trypanosoma brucei*. With our strain, such an inoculation produced an infection of the blood stream in twenty-four hours and death in from four to five days. In our experiments, we have followed the method of Voegtlin.[7] A series of animals were injected intraperitoneally with 0.5 c.c. of blood from a heavily infected rat. Twenty-four hours later the blood was examined. When the count had reached 150,000 per cubic millimeter, a point occurring in our experiments in forty-eight hours, disodium arsphenamin, or gelatin arsphenamin, was given in 0.5 per cent. solution intravenously. Doses of 5, 10, 20 and 30 mg. per kilogram were injected. Twenty-four hours later the blood was again examined for trypanosomes, and the examination repeated every day for eight weeks. In our experiments, we have determined both the "therapeutic dose" of Schamberg, Kolmer and Raiziss,[6] that is, the amount which prevents infection and which in this article we shall call the "minimum curative dose," and also the "minimum effective dose" of Voegtlin, which is the amount that clears the blood stream of parasites in twenty-four hours. Another modification in our procedure was to test only two or three animals with the same dose in a given experiment. Sufficient data for each dose was obtained by repetition of the experiments. Such a method is a more rigorous test than the treatment of all the animals of a given dosage at one time, as in such a procedure errors and uncontrolled factors may influence all the data concerning a given dosage. Table 2 gives the results of fifty-three treatments.

The minimum effective dose, that amount which clears the blood stream of infection in twenty-four hours, is found to be 10 mg. per kilogram for both gelatin arsphenamin and disodium arsphenamin. All the animals given such an amount of either form of the drug were found free from trypanosomes on the day following the treatment. Five milligrams per kilogram was insufficient, although the desired effect was found in some of the animals.

TABLE 3.—*Treatment of Experimental Trypanosomiasis with Disodium Arsphenamin and Gelatin Arsphenamin* *

Dose per Kilogram	Days After Treatement																									
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24		
Disodium arsphenamin = 5 mg.	−	−	−	−	−	−	−	±	+	+	++	D.														
	+	−	−	−	−	−	±	+	+	++	++	D.														
	±	−	−	−	−	−	−	+	+	++	++	D.														
	−	−	−	−	−	−	−	−	−	−	−	−	−	++	++	D.										
	−	−	−	−	−	−	−	−	−	−	−	−	−	+	+	+	+	++	++	D.						
	+	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	++	++	D.						
Gelatin arsphenamin	±	−	−	−	−	−	−	+	++	D.																
	−	−	−	−	−	−	−	−	−	+	++	D.														
	±	−	−	−	−	−	−	−	−	+	+	++	D.													
	−	−	−	−	−	−	−	−	−	+	+	++	++	D.												
	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	++	++	D.							
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	++	+	+	++	D.			
Disodium arsphenamin = 10 mg.	−	−	−	−	−	−	−	−	−	−	−	+	++	D.												
	−	−	−	−	−	−	−	−	−	−	−	+	+	+	++	D.										
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	++	D.		
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	25 +	29 D.
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
Gelatin arsphenamin	−	−	−	−	−	−	−	−	−	−	−	−	+	++	D.											
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	++	++	D.							
	−	−	−	−	−	−	−	−	−	−	−	−	−	+	−	−	±	+	+	++	++	D.				
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	++	++	++	D.				
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	+	++	D.		
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
Disodium arsphenamin = 20 mg.	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	33 +	38 D.
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	+	++	D.		
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	33 +	35 D.
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	37 +	45 D.
Gelatin arsphenamin	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	34 +	44 D.
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	30 +	33 D.
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−

* Seven animals treated with 30 mg. per kilogram of disodium arsphenamin and eight animals treated with the same dose of gelatin arsphenamin showed no trypanosomes on the following day and remained permanently cured. Untreated rats died in from three to four days.

The minimum curative dose differed for the two preparations. Whereas 20 mg. per kilogram of gelatin arsphenamin prevented relapse in more than half (five-sevenths) of the animals, this dosage of disodium arsphenamin was effective in only two-sevenths of the experiments. The relapses which occurred in both instances were late, occurring from thirty to thirty-seven days after treatment. Thirty milligrams per kilogram resulted in a complete cure of all the animals with both forms of the drug. The minimum curative dose for the majority of the animals is therefore 30 mg. per kilogram for disodium arsphenamin, and 20 mg. per kilogram for gelatin arsphenamin.

THE THERAPEUTIC EFFICIENCY OF DISODIUM ARSPHENAMIN AND GELATIN ARSPHENAMIN IN THE TREATMENT OF RABBIT SYPHILIS

Scrotal chancres were produced in a number of rabbits by inoculation of small bits of tissue from early untreated primary lesions in man. Three strains were thus acquired, and these were transplanted to a second generation by the same technic. Only typical, well formed, indurated chancres were used for treatment. Care was taken to avoid periods when cyclic changes, such as spontaneous regression, might occur. Seven animals were injected with gelatin arsphenamin in varying doses. The experimental results were as follows:

Results of Injection of 0.02 Gm. of Gelatin Arsphenamin per Kilogram of Body Weight.—Rabbit 280, Strain 217:

8/18/22: Inoculated in right scrotum.

10/11/22: Typical indurated chancre, 15 by 15 mm., with central ulceration covered by a scab. Twenty-five to 30 spirochetes in each dark field.

10/19/22: Sixty-two days after inoculation, lesion as described above with many spirochetes (Fig. 3A). Weight, 1.9 kilograms. Given 7.8 c.c. of 0.5 per cent. gelatin arsphenamin, equaling 0.02 gm. per kilogram.

10/20/22: No spirochetes found in spite of careful search.

10/21/22: Lesions much softer, edges wrinkled.

10/24/22: The induration had disappeared, the central scab measured 8 by 8 mm.

10/27/22: Superficial scab alone remained, 4 by 4 mm. in diameter (Fig. 3B).

10/30/22: Eleven days after treatment; skin smooth, complete healing (Fig. 3C).

12/20/22: No relapse.

Rabbit 224, Strain 217:

8/18/22: Inoculated in right scrotum.

9/7/22: Indurated nodule with beginning ulceration, 5 by 5 mm. Many spirochetes present.

9/20/22: Indurated chancre, 10 by 10 mm., with central ulceration.

10/19/22: Eighty days after inoculation, lesions measured 30 by 30 mm. with thick round indurated edges and a deep central ulceration covered with a scab (Fig. 4A). Many spirochetes present. Weight, 2.6 kilograms. Given 10.4 c.c. of 0.5 per cent. gelatin arsphenamin, equaling 0.02 gm. per kilogram.

10/20/22: Two nonmotile spirochetes found.

10/21/22: No spirochetes; the edge of the lesions is quite soft and wrinkled.

10/22/22: Some induration at base of central ulcer. Lesion measures 20 by 20 mm.
10/27/22: Slight induration beneath scab, 12 by 10 mm. in diameter (Fig. 4B).
10/30/22: No induration. Superficial scab measuring 6 by 6 mm. (Fig. 4C).
11/11/22: Twenty-three days after treatment, complete healing; slight puckering of skin from scar (Fig. 4D).
12/20/22: No relapse.

Results of Injection of 0.015 Gm. of Gelatin Arsphenamin per Kilogram of Body Weight.—Rabbit 232, Strain K4:
7/19/22: Inoculated in left scrotum.
7/10/22: Palpable nodule in skin.

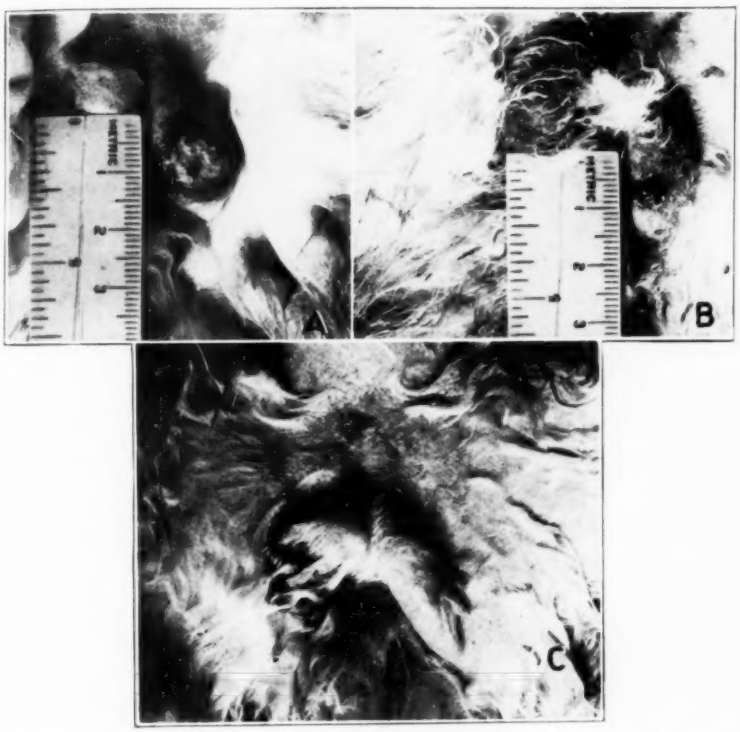

Fig. 3.—Rabbit 280, treated sixty-two days after inoculation with 0.02 gm. of gelatin arsphenamin per kilogram of weight. *A* shows the chancre on the day of treatment, measuring 15 by 15 mm., with indurated edge and central necrosis. *B*, eight days after treatment. There is no induration and the lesion consists of little more than a superficial scab, 4 by 4 mm. in diameter. *C*, eleven days after treatment, complete healing.

9/8/22: Fifty-eight days after inoculation, typical indurated chancre, 10 by 12 mm., with central necrosis. Many spirochetes present. Weight, 2.6 kilograms. Given 1.9 c.c. of 2 per cent. gelatin arsphenamin intravenously, equaling 0.015 gm. per kilogram.
9/9/22: No spirochetes found.

9/13/22: Induration gone, lesion consists of a superficial scab 3 by 3 mm. in diameter.

9/20/22: Twelve days after treatment. Skin smooth, complete healing.

12/20/22: No relapse.

Rabbit 245, Strain B:

7/17/22: Inoculated in right scrotum.

7/25/22: Palpable indurated nodule present.

8/31/22: Forty-four days after inoculation. Typical indurated chancre, 12 by 13 mm., with central ulceration and scab. Many spirochetes. Weight, 2.25 kilograms. Given 1.6 c.c. of 2 per cent. gelatin arsphenamin intravenously.

Fig. 4.—Rabbit 274, treated eighty days after inoculation with 0.02 gm. of gelatin arsphenamin per kilogram. *A* shows the chancre on the day of treatment, measuring 30 by 30 mm., with central necrosis. Note the thick round indurated edge. *B*, eight days after treatment. The indurated edge has entirely disappeared leaving only the central destroyed area covered with a scab. Healing from this time on is largely a matter of repair of this defect by granulation tissue and a replacement of the scab by regenerated skin. *C*, ten days after treatment. The scab has shrunken to 6 by 6 mm. in diameter. The testicle has resumed its normal shape. *D*, twenty-two days after treatment, complete healing. Owing to the large amount of destruction of tissue in this case, considerable puckering of the skin has been produced by the shrinkage of the granulation tissue.

9/2/22: No spirochetes found.
9/9/22: No induration, but a superficial scab 2 by 2 mm. in diameter.
9/13/22: Thirteen days after treatment, skin smooth, some pigmentation, but complete healing.
10/23/22: Died, multiple subcutaneous abscesses; no relapse.

Rabbit 277, Strain 217:
8/18/22: Inoculated in right scrotum.
9/8/22: Twenty-one days after inoculation, typical indurated chancre, 7 by 10 mm., with central ulceration. Many spirochetes. Weight, 2.8 kilograms. Given 2.1 c.c. of 2 per cent. gelatin arsphenamin, or 0.015 gm. per kilogram.
9/9/22: No spirochetes found.
9/13/22: Soft nodule, 3 by 3 mm., covered with superficial scab.
9/20/22: Twelve days after treatment. Skin smooth, complete healing.
12/20/22: No relapse.

Results of Injection of 0.005 Gm. of Gelatin Arsphenamin per Kilogram.—
Rabbit 276, Strain 217:
8/18/22: Inoculated in both sides of scrotum.
9/8/22: Twenty-one days after inoculation, bilateral chancres with indurated edges and central necrosis. Right side, 8 by 12 mm.; left, 10 by 10 mm. Many spirochetes in both. Weight, 2.7 kilograms. Given 0.77 c.c. of 2 per cent. gelatin arsphenamin intravenously, equaling 0.005 gm. per kilogram.
9/9/22: Occasional spirochetes found in each lesion.
9/10/22: No spirochetes found in either lesion.
9/13/22: Both lesions measured 8 by 8 mm., some induration.
9/20/22: No induration on either side, but superficial scabs.
10/20/22: Left side smooth, right side showed diffuse induration 4 by 4 mm.; relapse.

Rabbit 270, Strain 217:
8/18/22: Inoculated in right scrotum.
9/8/22: Twenty-one days after inoculation, typical indurated and ulcerated chancre, 8 by 5 mm. in diameter. Many spirochetes. Weight, 2.7 kilograms. Given 0.77 c.c. of 2 per cent. gelatin arsphenamin, equaling 0.005 gm. per kilogram.
9/9/22: No spirochetes found.
9/13/22: Induration decreased, lesion 5 by 5 mm. in diameter.
9/20/22: Old lesion healed.
10/18/22: A new nodule, 3 by 3 mm., beneath skin of right scrotum. Relapse.

The treatment with gelatin arsphenamin of three different strains of rabbit syphilis as manifested by typical chancres of from twenty-one to eighty days' duration, shows that it has a marked therapeutic effect. Compared with the findings of Ehrlich and Hata [3] and of Castelli,[4] it equals disodium arsphenamin in this respect. The minimum sterilizing dose of the latter is 0.015 gm. per kilogram, and although lesions may be healed with as little as 0.005 gm. per kilogram, relapses frequently occur.

The findings in the treatment of rabbit syphilis therefore agree with those observed in the treatment of experimental trypanosomiasis in indicating that gelatin arsphenamin is as effective therapeutically as disodium arsphenamin.

DISCUSSION

From the more exact results obtained in the treatment of experimental trypanosomiasis, certain quantitative comparisons can be drawn between the efficiency of disodium arsphenamin, neo-arsphenamin and gelatin arsphenamin. Such therapeutic indexes, in which the efficacy of the drug is compared to its toxicity, have been established for the first two mentioned arsenicals by Schamberg, Kolmer and Raiziss [6] and by Voegtlin.[7] The former have compared the maximum tolerated dose with the minimum curative dose, that amount which permanently cures the animal. The latter use the minimum lethal dose and the minimum effective dose, or that amount which frees the blood stream from parasites in twenty-four hours. We have used the data in the same manner as these two investigators so that our indexes are comparable to theirs.

We will first consider our findings with disodium arsphenamin and gelatin arsphenamin.

The minimum lethal dose of gelatin arsphenamin is 150 mg. per kilogram, the maximum tolerated dose, 140 mg. per kilogram. The therapeutic indexes are therefore:

$$\frac{\text{Minimum lethal dose, 150 mg.}}{\text{Minimum effective dose, 10 mg.}} = 15$$

or,

$$\frac{\text{Maximum tolerated dose, 140 mg.}}{\text{Minimum curative dose, 20 mg.}} = 7$$

For disodium arsphenamin, the following figures are found: The minimum lethal dose is 100 mg. per kilogram, the maximum tolerated dose, 90 mg. per kilogram. The indexes are:

$$\frac{\text{Minimum lethal dose, 100 mg.}}{\text{Minimum effective dose, 10 mg.}} = 10$$

or,

$$\frac{\text{Maximum tolerated dose, 90 mg.}}{\text{Minimum curative dose, 30 mg.}} = 3$$

We may now compare the indexes of gelatin arsphenamin with those of disodium arsphenamin, first, by means of the minimum effective dose,

$$\frac{\text{Therapeutic index gelatin arsphenamin, 15}}{\text{Therapeutic index disodium arsphenamin, 10}} = 1.5$$

or by using the minimum curative dose,

$$\frac{\text{Therapeutic index gelatin arsphenamin, 7}}{\text{Therapeutic index disodium arsphenamin, 3}} = 2.5$$

In either case there is a decided balance in favor of gelatin arsphenamin. It is one and a half or two and a half times as efficient as disodium arsphenamin, depending on whether the minimum effective dose or the minimum curative dose is taken as a basis for comparison.

This result may be compared with those of Schamberg, Kolmer and Raiziss and of Voegtlin, who, as has been stated, have made a

similar comparison between arsphenamin and neo-arsphenamin. Schamberg, Kolmer and Raiziss, using the minimum curative dose as a basis of calculation, come to the following conclusions: For arsphenamin,

$$\frac{\text{Maximum tolerated dose, 105 mg.}}{\text{Minimum curative dose, 23 mg.}} = 4.5$$

and for neo-arsphenamin,

$$\frac{\text{Maximum tolerated dose, 254 mg.}}{\text{Minimum curative dose, 40 mg.}} = 6.3$$

and comparing the two drugs,

$$\frac{\text{Therapeutic index neo-arsphenamin, 6.3}}{\text{Therapeutic index arsphenamin, 4.5}} = 1.4$$

Voegtlin, using the minimum effective dose, gives the following figures. For arsphenamin,

$$\frac{\text{Average minimum lethal dose}}{\text{Average minimum effective dose}} = 20$$

and for neo-arsphenamin,

$$\frac{\text{Average minimum lethal dose}}{\text{Average minimum effective dose}} = 24$$

Comparing the two drugs, we have,

$$\frac{\text{Therapeutic index neo-arsphenamin, 24}}{\text{Therapeutic index arsphenamin, 20}} = 1.2$$

There is a substantial agreement between the results of these investigators in the conclusion that neo-arsphenamin is from one and two tenths to one and one half times as efficient as arsphenamin. As we have stated, our results show an even greater advantage in favor of gelatin arsphenamin as compared to arsphenamin, for it is one and a half or two and one half times as efficient as the latter form of the drug, depending on whether the minimum effective or minimum curative dose was considered. We believe that the latter comparison is to be preferred, as the prevention of relapses is doubtless due to the delayed excretion of gelatin arsphenamin. Certainly in the treatment of human syphilis such a prolonged action is to be preferred to that of arsphenamin, which, as Voegtlin has shown, is rapidly excreted during the first twenty-four hours and whose therapeutic activity, for experimental trypanosomiasis at least, is largely limited to this period.

It will be noticed in the data given above that the therapeutic index for arsphenamin as determined by us is lower than that arrived at by Schamberg, Kolmer and Raiziss. This is due to the somewhat different technic of the two sets of experiments. In our tests, the blood stream infection was well established before treatment was started, whereas in their experiments treatment was given in many cases two days before the parasites had reached the blood stream. It is therefore not surprising that more arsphenamin was required in our experiments to cure the animals.

The data establishing the indexes and ratios discussed above may be summarized briefly. Gram for gram, gelatin arsphenamin is as effective, and under some conditions more effective than arsphenamin and only three fifths as toxic. Compared to the data of other investigators, it is twice as effective as neo-arsphenamin, gram for gram, and one and eight tenths times as toxic, disodium arsphenamin being two and four tenths times as toxic as neo-arsphenamin.

So far in this discussion the measure of toxicity, minimum lethal dose and maximum tolerated dose, has taken into account only the late chemical toxicity of the compounds. As we have previously shown,[1] the physical toxicity and the ill effects due to circulatory disturbances are absent with gelatin arsphenamin. There is considerable evidence (Hanzlik and Karsner,[8] Smith and Jackson,[9] Smith,[10] Pomaret,[11] Oliver and Yamada[12]) which indicates that these are the factors responsible for the immediate ill effects that may follow the injection of disodium arsphenamin. No mathematical comparison can be made using these toxic factors as a basis of calculation, since they vary with different animals. It may be stated, however, that while they are inherent in disodium arsphenamin and the possibility always exists that they may produce untoward results, in the equally effective gelatin arsphenamin they have been removed. Judging from the experimental evidence at hand, acute reactions should be avoided by its use with no sacrifice in the therapeutic efficacy.

CONCLUSIONS

1. Gelatin arsphenamin is somewhat less trypanocidal in vitro than disodium arsphenamin.

2. Gelatin arsphenamin is retained in the animal at a higher concentration for a longer period than is disodium arsphenamin.

3. Gelatin arsphenamin is as effective as disodium arsphenamin in the treatment of experimental trypanosomiasis and rabbit syphilis. Under certain conditions it is more effective.

4. Therapeutic indexes established on the basis of the late or chemical toxicity of the two preparations favor gelatin arsphenamin as compared to disodium arsphenamin.

5. The immediate toxic effects of disodium arsphenamin may be avoided under experimental conditions by the use of gelatin arsphenamin without any sacrifice in therapeutic efficiency.

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POIKILODERMA ATROPHICANS VASCULARE

CONCLUSION OF PREVIOUSLY REPORTED CASE *

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Two years ago I reported a case of poikiloderma atrophicans vasculare.[1] The patient was a man, 30 years old, whose body was largely covered with typical lesions of poikiloderma in various stages of development. The earliest lesions had started twelve years earlier. Illustrations of the various lesions and details of the history, which was carried to February, 1921, were given in that report and need not be repeated here.

The patient was not seen again until April 4, 1922, when he consulted me about a tumor of the right shoulder which had begun to appear four weeks before, and which was growing rapidly and was accompanied by some pain.

Over the front of the right shoulder, extending on to the chest below the clavicle and on to the upper part of the arm, there was a round, hard tumor about 10 cm. in diameter. It was about 3 cm. in thickness. There were two small superficial ulcerations on the surface, and several scars of healed ulcerations (Fig. 1, which should be compared with Figs. 1 and 4 of previous article[1]). There were no enlarged glands in the right axilla or elsewhere.

Otherwise the condition of the patient was little different than when previously seen. There had been an increase of the extent of the skin lesions, with new ulcerations on the much atrophied surfaces (Figs. 2 and 3), and there was a spot on the back which had greatly increased in size, and which showed all the varied lesions of poikiloderma, except ulceration (Fig. 4).

I was undecided as to the nature of the tumor, but had the impression that it was either sarcoma or a deep abscess, and sent the patient to the surgical service of the New Haven Hospital, where the diagnosis was not settled, as the patient left the hospital the following day.

Aspiration of the tumor revealed no pus. The blood examination disclosed 85 per cent. of hemoglobin, 4,800,000 red blood cells, 8,400 white blood cells, 71 per cent. polymorphonuclears, 17 per cent. lymphocytes, 8 per cent. large mononuclears and 4 per cent. eosinophils.

I did not see the patient again until Sept. 13, 1922, when I was able to see him through the courtesy of Dr. W. S. Lay, of Hamden, who knew of my interest in the case. He was seen on this date, with Dr. Lay and Dr. George Blumer, of New Haven. He had been quite sick for about a week, with a temperature of about 100 to 101 F., and at this time was in bed, lying on his back with his knees drawn up, complaining of intense burning and itching of the whole surface of the body, which was most severe on the scrotum. There was also burning of the mucous membranes of the nose, mouth and throat. The

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* Read at the Meeting of the American Dermatological Association, June 7 to 9, 1923.

1. Lane, J. E.: Poikiloderma Atrophicans Vasculare, Arch. of Dermat. & Syph. **4**:563 (Nov.) 1921 (Case 13).

patient was emaciated. The tumor over the right shoulder was not as prominent as when last seen but covered a larger area, and a large part of the pectoral muscle in the vicinity was evidently infiltrated by it. The only notable change in the appearance of the skin was the presence on the chest and abdomen of a large number of purple nodules about 1 cm. in diameter. These were not elevated, not hard, but distinctly palpable.

The additional physical findings are described by Dr. Blumer as: (1) Enlargement of the cervical, axillary and inguinal lymph nodes. The glands were discrete, moderately hard, somewhat tender and varied in diameter from 1.5 to 4 cm., the largest being in the right axilla. (2) An infiltrating swelling

Fig. 1.—Tumors on patients' right shoulder and arm.

over the anterior surface of the right shoulder and below the outer end of the right clavicle associated with a general enlargement of the right arm, doubtless from pressure on the axillary vein. The radial artery pulsated normally. (3) Restricted movement of the right side of the chest with skodaic resonance below the right clavicle. Dulness to flatness from apex to base in the right axilla and the same signs from the level of the spine of the scapula to the right base behind. Over these areas the fremitus was diminished to absent, and the voice sounds were distant and in places nasal. There was a small Grocco triangle on the left side, and the heart was slightly displaced to the left, the apex beat being 2 cm. outside of the nipple. (4) An enlarged spleen palpable just above the margin of the ribs, and distinctly harder than normal.

Blood examination revealed: hemoglobin, 95 per cent.; red blood cells, 4,976,000; white blood cells, 49,000; polymorphonuclears, 96.6 per cent.; small mononuclears, 1 per cent.; large mononuclears, 2.33 per cent.

Two days later (Sept. 15) the right pleural cavity was aspirated. The report of the findings by the Brady Laboratory of the New Haven Hospital

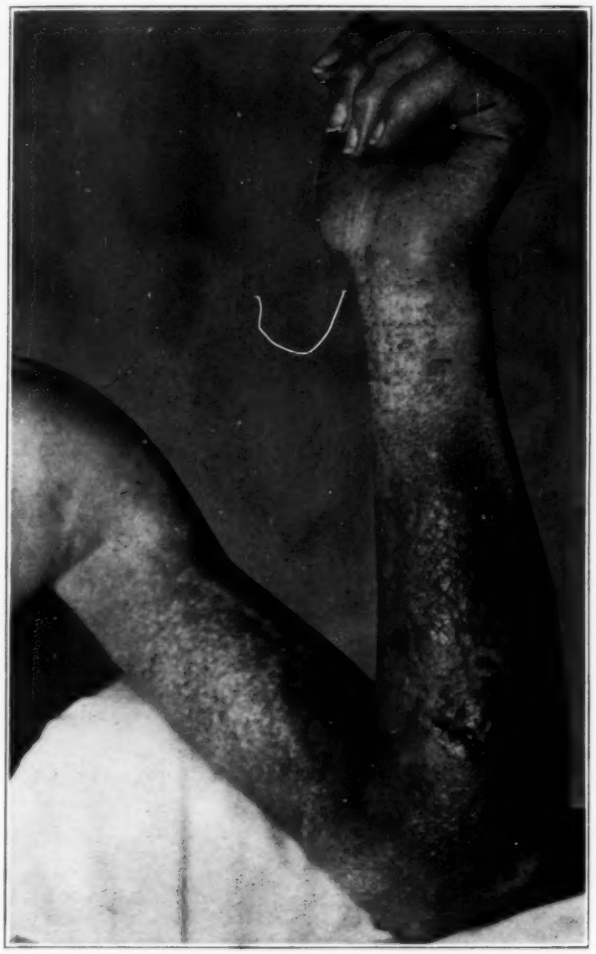

Fig. 2.—Ulcerations on arm.

was: albumin, 1.75 per cent.; numerous small lymphocytes, a few red blood corpuscles, occasional epithelial cells and sterile fluid. (The difference between these findings and those at necropsy should be noted.)

The diagnosis at this time was not definitely made. It lay between sarcomatosis and Hodgkin's disease, and Drs. Lay, Blumer and myself were inclined to accept sarcomatosis as the most probable.

The patient died on Sept. 18, 1922, and the necropsy was performed the same day at the Brady Laboratory of the New Haven Hospital. Owing to some misunderstanding, pieces of atrophic skin and of the small tumors on the chest were not removed. Permission for opening the skull was not obtained. The following report was given me by Dr. Woodruff Smith.

Fig. 3.—Ulceration on leg.

Anatomic Diagnosis.—Primary: (*a*) Hodgkin's disease (involvement of lymph glands, pleura, muscles, subcutaneous tissue and skin); (*b*) cellulitis of right thoracic wall and brachium; fibrinous pleurisy with effusion (*Streptococcus hemolyticus*).

Subsidiary: Poikiloderma atrophicans vasculare.

The subject was emaciated. He showed a striking brawny swelling of the anterior chest wall, shoulders and upper arm on the right side. Streptococci

were isolated from a cloudy fluid in the right pleural cavity, and were also seen in stains of tissue from the cervical lymph nodes and from the skin of the thorax and arm. The histologic picture of the indurated fasciae and muscles was that of an edematous granulation tissue infiltrated by polymorphonuclear leukocytes, including eosinophils, and by lymphocytes and plasma cells.

The lesions characterized as Hodgkin's disease consisted in a discrete enlargement of the lymphatic glands, excepting the follicles of the gastro-intestinal tract. There was an associated splenomegaly, and lesions believed to be a part of the same pathologic process were found as focal cell accumulations in the skin and deeper tissues of the thorax, and in granulation tissue of the right pleura at small points of adhesion between the lung and parietes. Suspicious cell groups were occasionally seen in the interstitial tissue of the pancreas.

The axillary and inguinal glands consisted of bilateral masses from 8 to 10 cm. in diameter, composed of individual nodes which were as large as 4 cm. Chains of similar glands enveloped the iliac vessels on both sides and were continuous throughout the retroperitoneal region to the mediastinum as far as the jugular notch. At the hilus of each lung the pulmonary tissue was compressed, though not invaded. In no instance was infiltration of a gland capsule noted. The glands were rather soft on section, with a glazed gray surface, in which at times small hemorrhagic areas were seen. Necrosis or fibrosis was not a striking part of the picture, either grossly or microscopically. The cervical glands were smaller than those just described, averaging 1 to 1.5 cm. in diameter. Many were pinkish and suggested grossly the picture seen in acute infections.

Even these cervical nodes were striking microscopically and appeared to represent an early stage of the lesion involving to such a marked degree the glands of the body cavities. The cortex was loose and vascular. Within it were irregular clumps of large mononucleated and binucleated cells.

These cells are quite similar to those classically described by Reed in Hodgkin's disease, but they are also not unlike the large and well preserved mononuclear cells which are observed, for instance, in the bronchial lymph glands of patients with pneumonia. Their cytoplasm is pink and homogeneous with hemotoxylin-eosin stains, while the nuclei, rounded or irregular in shape, are pale with a sharply blue staining nuclear membrane, two or three distinct nucleoli, and scattered chromatin granules. In the glands of this case, however, unlike an acute infection, the cells were characteristically present in the meshes of the cortical reticulum, and were not found free in the dilated sinuses. The sinuses were relatively empty, except for a loose fibrin network and scattered lymphocytes, as well as demonstrable long chained streptococci.

The huge, pale glands showed an almost complete replacement of the gland structure by a diffuse overgrowth of these cells, among which were numerous mitotic figures. Eosinophils were present, as well as polymorphonuclears and scattered lymphocytes. It must be noted that there was a slight increase in fibrous tissue, while practically no areas of necrosis could be found.

The spleen weighed 405 gm. and was 18 cm. long. It contained whitish nodules of varying size with indefinite borders, which were found to be composed principally of these large cells.

The lymphogranulomatous lesions of the other tissues may be summarized briefly. Beneath the epidermis of the skin, and deeper in the edematous tissue of the right thoracic wall, were minute, rounded nodules which were visible to the naked eye in stained sections. They were composed of lymphocytes

lying in a delicate connective tissue reticulum. Large mononuclear cells of the type described were found in these nodules, together with a lesser number of eosinophilic and neutrophilic leukocytes. Whitish nodules were seen grossly in the left pectoral muscle, which was uninvolved by the acute infec-

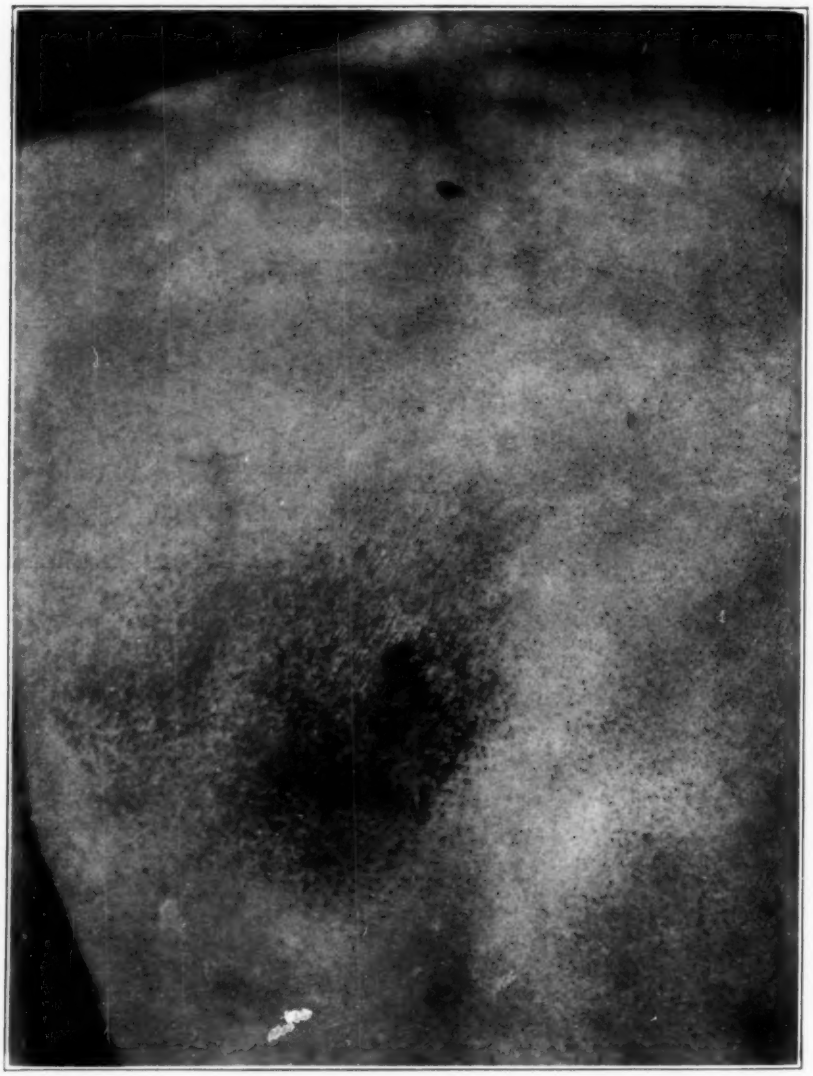

Fig. 4.—Poikiloderma on patients' back.

tious process. They measured from 1 to 2 mm. in diameter and were found to be similar structurally to the nodules in the skin. Here, though the nodules were fairly well defined, no fibrous wall or line of demarcation existed to separate the lesion from the surrounding muscle, which showed gradually fading

lymphocytic infiltration. In the pleural granulation tissue similar lymphocytic clumps were less clearly defined, while in the interstitial tissue of the pancreas there were simply focal points of round cell infiltration containing a few large mononuclear cells.

It is interesting that in these briefly described lesions of the lymphatic system and other tissues, streptococci or other organisms could not be identified, except in the cellulitis of the thoracic wall and in the sinuses of the cervical lymph node. The methods employed were Giemsa's method, stains for acid-fast organisms, and the ordinary bacteriologic dyes.

In addition to the lymphogranulomatous nodules of the skin, the epidermal layer was in general thin. The papillae of the corium were lacking over extensive microscopic areas, or the base of the malpighian layer presented simply an undulating border. Congestion of the terminal capillaries was often striking, while vascular loops lined only by endothelium appeared to invade the squamous cells so as to be extremely near the surface. Here often the horny layer was either absent or very thin.

CASES REPORTED IN THE LITERATURE

The conclusion of this case is of interest from the rapid development of Hodgkin's disease, and from the fact that the first discoverable growth was in the vicinity of an ulcer in an atrophic area of poikiloderma. This ulcer was also apparently the point of entry of *Streptococcus hemolyticus*, which was the immediate cause of death.

This is the third patient with poikiloderma who has come to necropsy. The first, that of Petges and Cléjat,[2] died of tuberculosis of the lungs; Ormsby's,[3] the second patient, died of generalized lymphosarcoma.

Since the publication of my previous article, several cases of poikiloderma have been reported, and there have been several more in which the diagnosis was in doubt, or in which the condition was so similar as to suggest poikiloderma. A detailed study of these cannot be made at this time. I will briefly refer to them in order to bring the bibliography up to date.

Flehme [4] reported a case of poikiloderma in a woman, aged 34, of seven years' duration, in which the whole body, with the exception of the face, legs and feet, was affected.

Cappelli's [5] patient was a married woman, aged 28, who had had the disease three years. It started three weeks after childbirth. The Was-

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2. Petges and Cléjat: Sclérose atrophique de la peau et myosite généralisée, Ann. de dermat. et syph. **7**:550, 1906.

3. Lane, J. E.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **4**:563 (Nov.) 1921 (Case 14).

4. Flehme, E.: Ueber einen Fall von Poikilodermie atrophicans vascularis, Arch. f. Dermat. u. Syph. **135**:156, 1921.

5. Cappelli, J.: Poichilodermia atrophicans vascularis, "Jacobi," (Communicazione preventiva), Gior. ital. d. mal. ven. **63**:617, 1922. (Case reported at Societa Ital. di Dermatologia e Sifilografia, Roma, 15-17, December, 1921).

sermann reaction was negative, the cutaneous tuberculin reaction positive, the sella turcica normal. There was slight exophthalmos and slight enlargement of the left half of the thyroid.

Wertheimer's [6] patient was a man, aged 46, in whom the disease had made its appearance twenty-five years previous. The diagnosis was agreed to by Drs. Fred Wise and Howard Fox.

Whitehouse's [7] patient was a married woman, aged 34, born in Bohemia, who had had the disease for fourteen years. The diagnosis of poikiloderma was accepted by those who saw the patient.

The cases above cited are probably properly classed as poikiloderma atrophicans vasculare. The following cases presented somewhat similar conditions, but their proper classification is doubtful.

Burns' [8] patient was a man, age not stated, whose disorder began fifteen years before. The process was characterized by infiltrated papular lesions, followed almost invariably by a certain amount of atrophy. No positive diagnosis was suggested in this case.

H. R. Foerster [9] showed a man, aged 58, with a condition resembling poikiloderma, which had been present two years. No diagnosis was suggested, though there was agreement that it was not poikiloderma.

C. Guy Lane's [10] patient was a woman, aged 27, who had had pruritus for four years. There were peculiar bright read areas on the neck, about the waist and also on the buttocks, with a peculiar reticulated appearance.

Civatte [11] reported three cases of a variegated eruption of the face and neck, to which he gives the name of reticulated and pigmentary poikiloderma of the face and neck, but which he differentiates from the poikiloderma of the Jacobi type. This disease Civatte thinks may be due to endocrine trouble. Two of his patients were improved by the use of epinephrin.

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6. Wertheimer: Poikiloderma Vascularis Atrophicans, Arch. Dermat. & Syph. **6**:252 (Aug.) 1922. (Case shown at Pittsburgh Dermatological Society, April 27, 1922.)

7. Whitehouse, H. H.: Arch. Dermat. & Syph. **7**:836 (June) 1923.

8. Burns: Generalized Dermatosis, Arch. Dermat. & Syph. **4**:556 (Oct.) 1921. (Case shown at American Dermatological Association, June 2-4, 1921.)

9. Foerster, H. R.: A Case for Diagnosis, Arch. Dermat. & Syph. **5**:786 (June) 1922. (Case shown at Chicago Dermatological Society, Feb. 14, 1922.)

10. Lane, C. Guy: A Case for Diagnosis. (Poikiloderma Atrophicans Vasculare?), Arch. Dermat. & Syph. **7**:547 (April) 1923. (Case shown at New England Dermatological Society, Oct. 11, 1922.)

11. Civatte: La poikilodermie réticulée pigmentaire du visage et du cou, Presse méd. **30**:572, 1922. (I Cong. des dermat. et syphilig. de langue française, Paris, Jun 6-8, 1922.)

Ducrey [12] reported a case of a condition, dermatitis chronica atrophicans, of probable tuberculous origin, which he differentiates from Herxheimer's acrodermatitis chronica atrophicans and from poikiloderma.

Oppenheim [13] reported a case resembling poikiloderma, in which the histologic study showed typical dermatitis atrophicans.

Zeisler's [14] patient was a woman, aged 42 years, who had had the trouble for thirty years. From the neck down, the body and extremities were covered with a telangiectatic purplish red network, arranged in meshes and rings, and showed a reticulate atrophy with apparent loss of elastic tissue.

Not much light is thrown on the classification or etiology of poikiloderma by the study of these cases. Oppenheim believes that poikiloderma should be classed under the idiopathic atrophies, as does Capelli.

Capelli believes endocrine disturbance (thyroid) was an etiologic factor in his case.

The remaining cases of poikiloderma in which other diseases were associated suggest no etiologic relationship.

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12. Ducrey, C.: Dermatitis cronica atrophicans, di probabile natura tubercolare, Gior. ital. d. mal. ven. **63**:596, 1922. (Società Ital. di Dermatologia e Sifilografia, Dec. 15-17, 1921.)

13. Oppenheim, M.: Atrophia Cutis idiopathica progressiva universalis, Zentralbl. f. Haut. u. Geschlichtskrankh. **2**:2 1921. (Wien. Dermat. Gesellsch. Sitz V, May, 9, 1921.)

14. Zeisler: Poikiloderma atrophicans vasculare: Jacobi's Disease, Arch. Dermat. & Syph. **7**:709, 1923. (Case shown at Chicago Dermatological Society, Jan. 17, 1923.)

KERATOSIS PALMARIS ET PLANTARIS DUE TO FRAMBESIA *

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MANILA, P. I.

Late lesions of yaws affecting the palms and soles have been reported in the literature, but the authors who made these observations do not give us a clear and concise idea of these lesions. This article is an attempt to give a clear picture of these conditions so common in countries where yaws is prevalent. Only lesions affecting the palms and soles accompanied by a hyperkeratosis will be discussed.

REVIEW OF THE LITERATURE

The literature is replete with references to other types of tertiary lesions of yaws, but I have found only two articles dealing with tertiary lesions of the palms and soles. Castellani [1] calls attention to a "peculiar pitted appearance of the palms of the hands." This condition, he states, is manifested in the "latter part of the secondary stage" as "hard, round, flattened papules or small nodules, having a thick, hard epidermic plug in the center. The condition may remain for years after all symptoms of frambesia have disappeared." Howard,[2] in Zanzibar, speaking of tertiary manifestations in general, says: "More often there is an absence of an interval of apparent complete cure for five to ten years and perhaps during this time the whole body is clear of rash, but there is the persistence of that chronic condition of the soles of the feet known as foot yaws (mitembo)."

FREQUENCY

Of the different late manifestations of the disease, this is the most common encountered in communities where yaws has been prevalent for some time. In our yaws clinic at Ilocos Norte, where we treated more than 1,200 patients suffering from this disease in its active or secondary stage, we found many people presenting themselves for treatment with this form of lesion. In the first 658 patients with active cases of yaws treated, the number accompanied by keratosis were

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* From the Department of Medicine, College of Medicine and Surgery, University of the Philippines.

1. Castellani and Chalmers: Manual of Tropical Medicine, Ed. 3, New York, William Wood & Co., p. 1550.

2. Howard, R.: The Importance of Tertiary Yaws, J. Tropical M. **18**:25, 1915.

recorded in an endeavor to ascertain their frequency. We found 431 people suffering from this type of lesion; in twenty cases there were ulcers and in twenty-three the bones were involved. Over one half of the patients that came to the clinic for treatment, therefore, were suffering from this type of lesion, while we encountered only forty-three patients suffering from other types of tertiary lesions. It is not meant to convey the impression that over 50 per cent. of all the people who

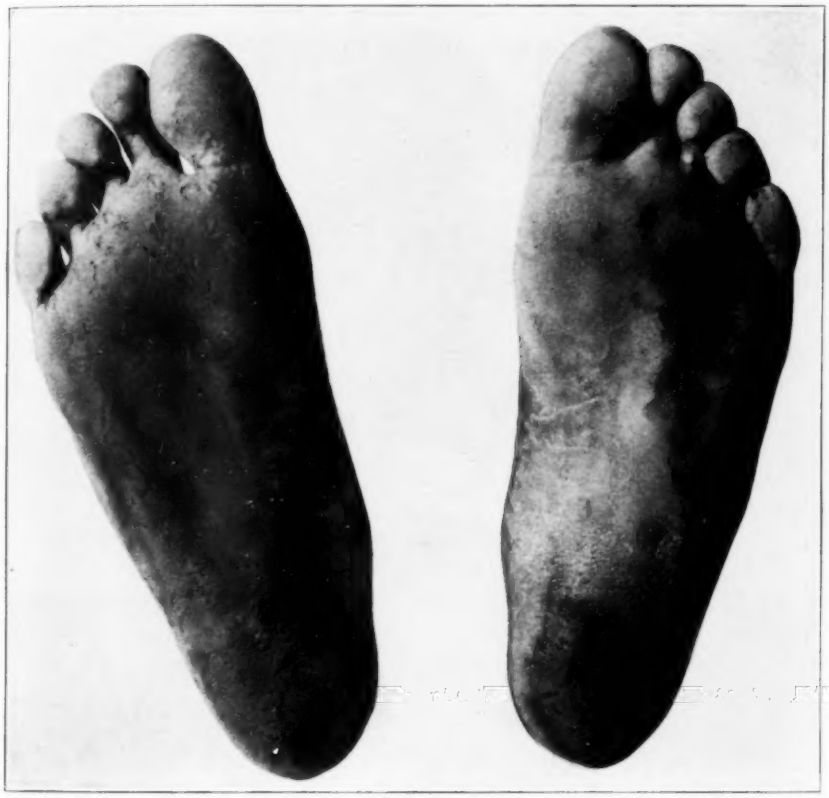

Fig. 1. (Case 1).—The patient had yaws one year ago. He had had the lesions six months. The picture was taken before treatment.

have had yaws will develop keratosis, as this can only be determined by following up patients who have had the disease, several years after the active lesions have healed. The foregoing figures, however, show us the frequency of these lesions in a community where yaws has been prevalent.

That these lesions are the result of a previous infection of yaws there can be no doubt. In nearly all of our cases, we obtained a history

of a previous attack of yaws. In the few in which a history could not be obtained, the lesions were so typical and the response to treatment so prompt that it leaves no doubt as to the nature of the disease. These persons could easily have had yaws during childhood and have forgotten it or were not aware of it, as is usually the case among the poor.

TYPES OF LESIONS

We have observed two main types of lesions. One type is shown in Figure 1, in which there is pitting left by sago-like hardened corneum, which we have designated as claviform keratosis; the other is simply a thickening of the corneal layer without the special formation of these bodies, as depicted in Figure 2.

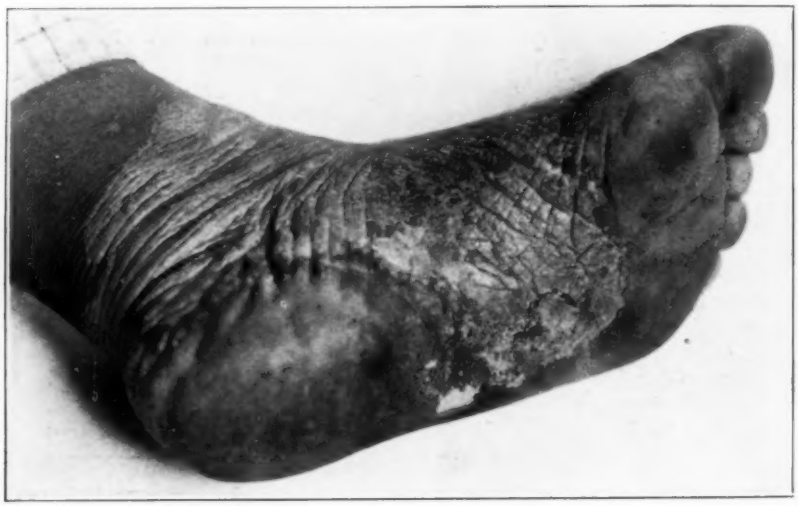

Fig. 2.—Plantar lesions of the keratotic type. The patient had yaws five years ago.

The lesions may appear during the latter part of the secondary stage, or they may appear twenty-four years after the disease has seemingly healed. Usually, however, there is an interval of from one to five years before the appearance of this condition, during which time all symptoms of the disease may have disappeared.

The lesions appear gradually, at first manifested by a hyperpigmentation of one or both palms or soles. This hyperpigmentation may last for months before the person notices slight thickening taking the place of the hyperpigmentation. The keratosis gradually becomes more marked, surrounded by areas of hyperpigmentation. The lesion enlarges peripherally, extending over the hyperpigmented area, and in

this way it gradually extends over the entire palm or sole. As a consequence of this thickening, motion becomes difficult and fissures appear about the joints.

From the palmar or plantar aspect, the disease gradually extends toward the sides and back (Figs. 3 and 4). The disease may encroach and involve the entire back of the hand in a solid patch. On the other hand, this involvement may be confined to the joints of the phalanges

Figure 3

Figure 4

Fig. 3.—Palmar lesions of the keratotic type.
Fig. 4.—Dorsum of hand in palmar lesions of the keratotic type.

and metacarpals. These become thickened, scales are formed and shed and the process extends. In the same manner the wrists and elbows are involved, and on the feet the dorsal aspect and ankles are also affected.

The pigment over the keratotic areas later disappears as a further progress of the disease (Fig. 5). These leukodermic spots at first are

discrete, but sooner or later they become confluent, and in this way the whole back of the hand or dorsum of the foot may be depigmented. When the process has reached this stage, the skin may lose the hyperkeratotic quality heretofore present; the texture becomes more or less normal, except in those places in which the leukoderma is not manifest. When the entire palm or back of the hand is devoid of pigment, there are usually patches of intensely pigmented islands in the leukodermic areas.

Closely related to this form is another type composed of hyperkeratotic patches whose margins are red and elevated. Keratosis is confined to the edges where scaling is also a marked feature. As the process extends, the center becomes more or less clear; the skin over this area becomes thinner, but it does not return to its normal texture;

Fig. 5.—Involvement of the dorsum of the foot; depigmentation.

the thickening returns as the scales are shed. Later, depigmentation like that in the foregoing type also becomes a feature. As in the foregoing, one or all of the extremities may be involved.

The other form mentioned above starts as hyperkeratosis in which are embedded corn-like whorls of hardened corneum (Figs. 1 and 9). These whorls are about the size of a grain of sago and are embedded in the corneal layer, their base nearly reaching the rete. They drop off spontaneously, leaving small pit marks scattered over the thickened palmar or plantar aspect. This condition is especially painful on walking because of the cornlike wedge which, like the corn, impinges on the sensitive corium.

During the rainy season, or when the feet have been continuously in water for days, subcutaneous nodules appear on the plantar surface,

which later become open sores, and which disappear during the dry season. These nodules are extremely painful, preventing the patients from working.

THE WASSERMANN TEST

The Wassermann reaction is variable, as in tests of persons with late syphilitic affections. It may be negative or slightly positive in late cases, that is, in those cases in which the active lesions of yaws disappeared ten or fifteen years ago; and the reaction may be strongly positive in those in which the secondary lesions have recently disappeared. The number of cases herewith reported are too few to warrant a discussion as to the frequency of a positive Wassermann reaction.

Results of Wassermann Test in Various Cases of Yaws

Case	Diagnosis	Duration of Lesions	Age at Which Patient Had Yaws	Wassermann Test
49	Keratosis	5 years	12 years	Negative
466	Claviform	6 months	1 year	++++
999	Keratosis	3 years	16 years	Negative
124	Keratosis	11 years	11 years	++
147	Keratosis	3 years	16 years	Negative
177	Claviform	2 years	6 years	++
250	Keratosis	7 years	24 years	Negative
310	Keratosis	12 years	20 years	++
350	Keratosis	8 months	1 year	+
402	Keratosis	1 year	1 year	Negative

HISTOPATHOLOGY

As in the secondary lesions, the changes are confined to the epidermis and corium. In this condition, however, the changes are found mainly in the corneal layer and are manifested as hyperkeratosis. The corneal layer may be from five to ten times or more than its normal thickness (Fig. 6). The outlines of the individual cells are hard to make out, the mass of keratinized cells being compact and homogeneous. In places, however, the cells are separated by spaces formed in the mass itself. The clavus is composed of laminated horny cells, interspersed with parakeratotic cells. These cells are compact, forming a body more or less rounded and separated from the rest of the horny keratotic cells beneath by spaces and loose layers of cells around the base. This body is easily separated from the keratotic mass by the arrangement mentioned in the foregoing, and when shed off, it leaves a cuplike depression almost reaching the rete. Its shape is rounded. Its top projects slightly above the surface of the skin. On superficial examination, these bodies may appear like small vesicles similar to those found in pompholyx, but on attempting to puncture them they will be found to be solid masses of horny cells. The sweat pores are patent even in the thickest portion of the keratotic skin.

Fig. 6.—Section of a cornlike keratosis; low power magnification.

Fig. 7.—Section beneath the cornlike body under high power magnification.

The stratum lucidum is clearly perceived. The granular layer is thickened, being from five to eight layers thick. The thickening is not uniform even in the same section. This difference in thickness is probably due to the difference in pressure in the different portions of the skin. I have not observed the thickening to be more marked under the

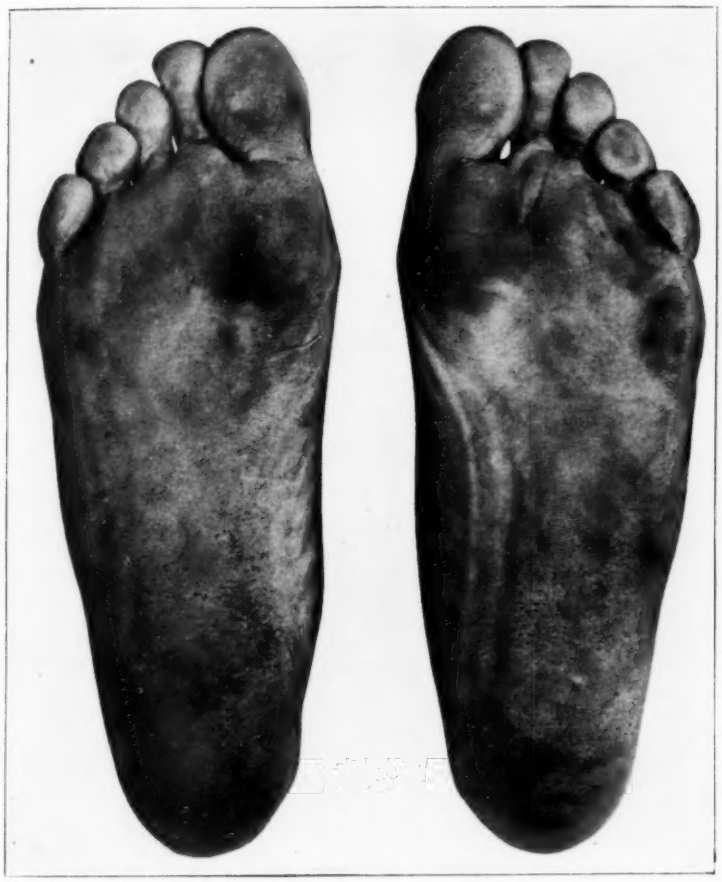

Fig. 8 (Case 1, Fig. 1).—Two months after treatment.

cornlike formation than in other places; in fact, I found the granular layer thinner in this portion of the skin.

The acanthosis is not as marked as that found in the lesions of the secondary stage of the disease. The thickening is, however, sufficiently marked to call instant attention to it. There is no infiltration in the rete, nor are there small miliary abscesses in it, as observed in the secondary lesions (Fig. 7).

Some of the papillae are flattened and some hypertrophied, probably owing to pressure from without and within. There is edema in the papillary and subpapillary layer. There are no changes in the vessel walls.

The infiltration is confined to the papillary layer and to a certain extent to the region of the blood vessels. The infiltration is composed mainly of plasma cells and a few round cells.

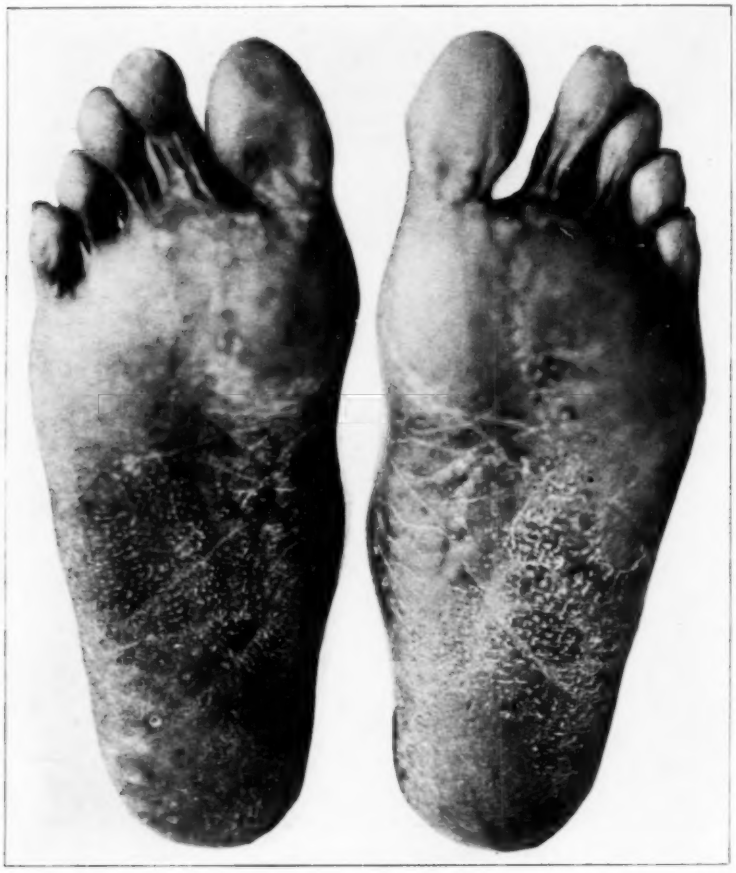

Fig. 9. (Case 3).—Before treatment.

REPORT OF CASES

Case 1.—Six months ago, F. A. (Case 466, Figs. 1 and 8) noticed that his soles were getting thicker. With this thickening, he noticed small, hard, cornlike bodies which caused him pain when he walked. The pain was especially marked when he was barefooted. The palms were also involved. On these, the skin was thickened and peeled as it became thick, but the thickening was maintained by proliferation of the corneal layer. The knuckles were involved.

On the lateral aspects of the hands, there were cornlike bodies. These dropped off, leaving pinhead sized depressions. According to one of the resident physicians, the patient had yaws in 1920. The Wassermann reaction was four plus. The patient was given a dose of arsphenamin, 0.46 gm., on August 5. On August 12, the lesions were much better; desquamation was noted and the skin was becoming softer. On August 24, the skin was

Fig. 10. (Case 3).—After two months in the hospital and after three injections of neo-arsphenamin.

much improved. The skin on the hands was normal in texture. On September 16, the plantar surfaces were found to be normal in texture, except for the pitting, and on December 7, even the pitting had disappeared. From the beginning of the treatment to the time the skin became normal was exactly one year. Three injections of neo-arsphenamin were given at intervals of three weeks. With neo-arsphenamin, iodids and mercury were given.

CASE 2.—M. L. (Case 602), had lesions which were of nine months' duration, localized on the plantar surface of both feet, involving the middle portion of the plantar surface and extending to the dorsum up to the ankle. There was considerable thickening and scaling. There were fissures about the articulations. The patient had had yaws when she was 7 years old; she is now 25. The Wassermann reaction was slightly positive. No treatment was instituted as the patient disappeared.

CASE 3.—B. D. (Figs. 9 and 10), a Filipino 40 years old, married, was admitted to the hospital for a disease unrelated to the present condition. Examination, however, revealed that the soles were very much thickened, scaly and presented roundish opaque areas varying in size from that of a pencil point to that of a pinhead. These opaque areas resembled corns, and when taken out left a pit. They were tender to pressure, and when the patient stood on her bare feet, she felt as though she were standing on the points of blunt nails. The skin around the sides as well as on parts of the dorsa of the feet was white and scaly. The natural lines of the skin were exaggerated. The Wassermann reaction was negative on two occasions. The patient did not remember having had yaws, but she came from a region where this disease was prevalent. She was given three injections of neo-arsphenamin of 0.45 gm. each and one of arsphenamin of 0.3 gm. She was also given iodids and mercury. After three injections and a stay in the hospital of about two months, there was an improvement of about 80 per cent. (Fig. 10). When she left the hospital, five months later, the lesions on the feet were practically well.

TREATMENT

In most of our cases we have used iodids with or previous to the injection of arsphenamin. This was done on account of the encouraging results obtained from the use of iodids alone in the latter stages of the disease. In all of our cases the disease yielded to arsphenamin or neo-arsphenamin. These were given from one to three weeks apart. Improvement is extremely slow with any form of treatment, requiring months, and in one case one year, before a complete return of the skin to normal was noticed. In the advanced cases where there was depigmentation, the skin returned to its normal texture, but in only one of the cases did the pigment return in the depigmented areas. It is, of course, too early to say that the pigment will not return in the other case, as there has not been sufficient time to observe these cases thoroughly.[3]

3. As this paper was being prepared, notice was called to an article by Moss and Bigelow (W. L. Moss and G. H. Bigelow: Bull. Johns Hopkins Hosp. **33**:43, 1922) on yaws in the Dominican Republic. These tertiary lesions were also described under the name of "clavus" on account of the sensation which the natives described as a feeling as though a nail has been embedded under the skin. The description of the etiology and the stage to which these lesions belong is at variance with our observations.

GONORRHEAL KERATODERMA *

REPORT OF A CASE

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AND
ERWIN P. ZEISLER, M.D.
CHICAGO

Gonorrheal keratoderma with generalized lesions is of sufficient interest to warrant the subjoined report.

CASE REPORT

History.—T. M., aged 29, single, a clerk, entered Cook County Hospital on June 23, 1922, with a urethral discharge and a painful swelling of several joints. Six weeks before entrance, he first noticed the urethral discharge accompanied by the usual symptoms of an acute gonorrheal urethritis. One week later the discharge stopped, and the right shoulder joint became painful on motion and tender to the touch. Two days later pain and swelling commenced in the jaw on the right side, and similar symptoms developed in the right knee and ankle. His past history was negative. The left limb was amputated at the thigh early in life, following an accident.

Physical Examination.—At the time of admission the temperature was 101 F., the pulse rate 78, and respiration 20. The patient was a well developed white man. The essential lesions included an enlarged prostate, a bilateral vesiculitis, and painful arthritis of the right ankle, knee, shoulder joint and jaw. The two glass test showed turbidity of both glasses. Examination of the urinary sediment and prostatic secretion showed the gonococcus both in smears and cultures. The diagnosis made in the urologic service by Drs. Culver and Phifer, to whom we are indebted for permission to report the case, was a subacute anterior and posterior gonorrheal urethritis, prostatitis and vesiculitis and multiple gonorrheal arthritis. There was no cardiac involvement.

Subsequent Course.—Local treatment was begun, and on June 28 a foreign protein (typhoid vaccine) was injected intravenously. On July 1, a seropurulent secretion was noticed in the conjunctival sac of the left eye, but no gonococci were found. On July 5 (six weeks after the onset of the arthritis), a papular eruption was first noticed on the upper part of the thigh and gluteal region. Within the next few days scattered lesions appeared on the right knee, the plantar surface and upper part of the abdomen. Within the following week new lesions had developed in the genital region, around the malleoli, dorsum of the foot, nails of the foot and hand, and lastly on the cheeks and scalp. The lesions on the body were first discrete, firm reddish papules, covered with a hard crust, while those on the sole were round, conical excrescences with a peculiar horny translucence which became enormously thickened in a short time.

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Description of Skin Lesions.—The entire plantar surface, with the exception of a clear zone at the instep, was occupied by brown, horny, conical masses, the whole giving the typical "relief map" appearance which was first described by the French authors. Individual lesions were from 1 to 3 cm. in diameter, in the form of blunted cones, almost rupial, with a peculiar yellowish-brown

Fig. 1.—Keratodermic sandal.

translucence, and were surrounded by a narrow hyperemic zone. On removal of the firmly attached horny plate, a moist reddened surface remained. Isolated waxy conical lesions from 3 to 4 mm. in diameter were found along the inner and outer plantar margins, on the dorsum of the foot and at the base of the fourth and fifth toe nail. The nail plates were thickened and discolored. There

was a marked swelling of the metatarsophalangeal joint. The right knee joint was enlarged, and over the knee cap were half a dozen papular yellowish brown lesions covered with a thick, horny crust. The glans penis showed a circinate balanitis. The shaft of the penis, scrotum, adjacent inguinal regions and stump of the thigh were occupied by an erythematopapular confluent eruption with a gray adherent crusts. Isolated lesions on the thigh varied up to 2 cm. in diameter. There were no bleeding points on removal of the crust and no pus, a reddish slightly infiltrated base remaining. A few small lesions of a similar type were found on the abdomen and around the left elbow. The palms were not involved. The finger nails showed a brownish discoloration due to a granular subungual deposit beneath the distal border. At the base of the thumb and right index finger were pea sized, waxy, keratotic papules. The first and second metacarpal joints and the distal phalanges of the right index finger and thumb were swollen and tender.

Fig. 2.—Involvement of finger nails and phalanges.

The eruption at the border of the scalp resembled a corona seborrheica. The greater part of the scalp was covered with a dirty grayish, heavily crusted, erythematous eruption. At the bridge of the nose, on the right cheek and on the chin were grouped, coin-sized, crusted lesions. The mucous membranes were free.

The patient remained in the hospital for approximately three months. By the middle of August, the eruption showed evident signs of retrogression. The nails became distintegrated by the subungual growth and dropped off. The horny "carapace" on the soles came off spontaneously. The keratotic lesions on the scalp, face, knees and genital regions underwent complete involution by the end of August, leaving the skin normal. During the entire course of the eruption no local treatment was used. The arthritis and urethral infection subsided simultaneously with the skin manifestations. There was no evidence of recurrence of the skin lesions when seen several months later.

Histopathology.—Pieces of tissue were removed from the plantar surface and the amputation stump. The epidermis was edematous, stained poorly, the cell were swollen and the intercellular spaces dilated. Leukocytes were seen here and there between the epithelial cells. Parakeratosis was marked, the granular layer being present only here and there. In the horny crust, alternating layers of nucleated and non-nucleated cells were found, and some serum under the crust, but no groups of leukocytes. The papillae were lengthened and bent, the interpapillary pegs correspondingly enlarged. The vessels of the papillary layer were dilated and surrounded by an infiltrate of leukocytes, round cells, epithelioid cells and a considerable number of mast cells. A few typical plasma cells were seen, and a good many smaller cells with an eccentrically placed

Fig. 3.—Unilateral involvement of the face.

wheel-like nucleus, which we could not definitely class as plasma cells. A similar infiltrate, much less marked, was seen about the deeper vessels and glands. No organisms could be demonstrated.

Our purpose in adding this apparently typical case of gonorrheal keratoderma to those already reported in the literature is to emphasize again certain differences between the keratotic eruptions occurring as a complication of severe gonoccocus arthritis and the atypical rupioid and crustaceous forms of psoriasis which have been reported in connection with joint lesions, the so-called arthropathic psoriasis. In 1920, Adamson [1] in an article entitled "Keratoderma Blennorhagica: Is It a

1. Adamson, H. G.: Brit. J. Dermat. & Syph. **32**:183 (June) 1920.

Form of Psoriasis?" reported several instances of rheumatoid arthritis associated with more or less extensive psoriasis of the limbs and trunk, with lesions on the soles resembling the heaped-up, horny-looking cones of "gonorrheal hyperkeratosis." According to Adamson, this clinical similarity was also noted by Waelsch, and the cases of keratosis blenorrhagica reported by Graham Little, Colcott Fox, Williams and Giles bore a superficial resemblance to psoriasis vulgaris. The histologic resemblance noted by Chauffard has also been found by other observers,

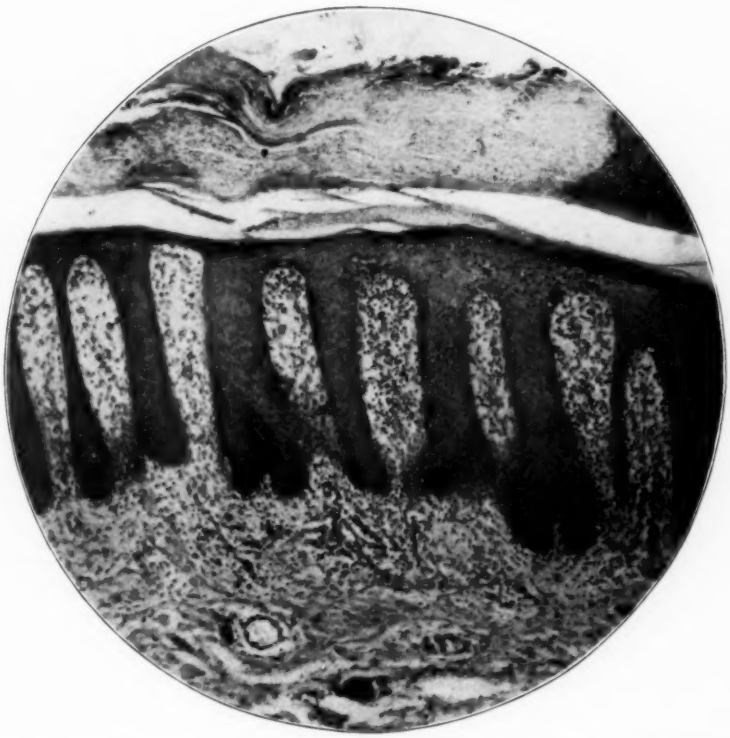

Fig. 4.—Parakeratosis, acanthosis and dilated blood vessels; thin epidermis above the papillae.

including ourselves, the changes in the horny layer being parakeratosis rather than hyperkeratosis. Several French authors (Balzer and Hallopeau) have also reported an atypical psoriatic eruption in cases of arthritis giving a history of gonorrhea. Adamson concludes "(1) that there are cases of arthropathic psoriasis in which lesions on the palms and soles strikingly resemble those of gonorrheal hyperkeratosis; (2) in many cases of gonorrheal hyperkeratosis there are eruptions of the limbs and trunk indistinguishable from psoriasis; (3) there are cases in which

it is difficult to make a differential diagnosis between arthropathic psoriasis and gonorrheal hyperkeratosis; and (4) there is a close similarity histologically."

Falk [2] in a recent article on psoriasis arthropathica would include in this category all cases of so-called "hyperkeratotic exanthems" in gonorrheal joint affections. He records a number of cases of arthropathic psoriasis in which the skin lesions were distinctly atypical both as regards location and character. The psoriatic lesions were found on

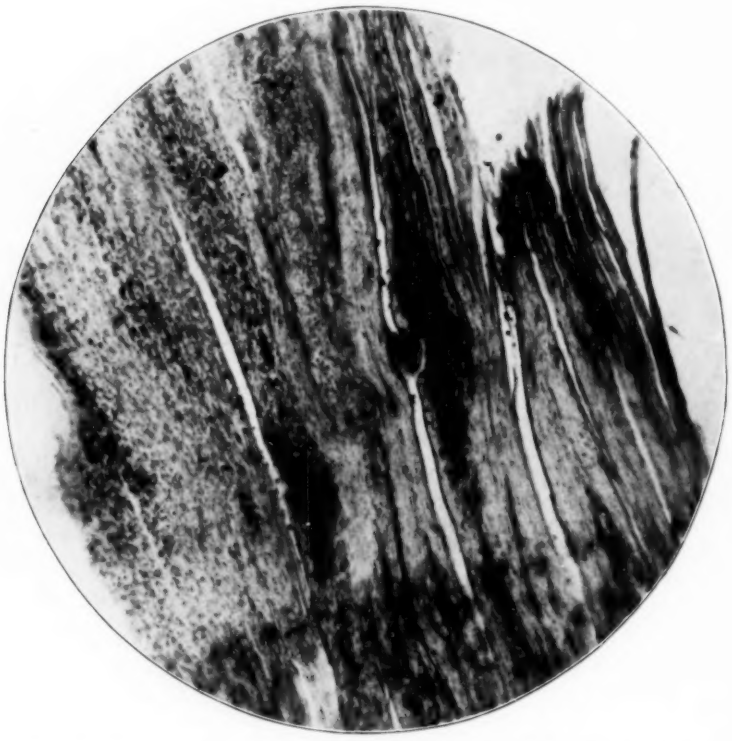

Fig. 5.—Alternating nucleated and non-nucleated layers in crust.

the palms and soles and around the penis, and the involvement of the nails was more constant and severe. The eruption was, furthermore, characterized by a greater degree of infiltration than normal, and by an unusual exudative tendency, instead of scales, crusts covered the lesions, their concentric arrangement suggesting syphilitic rupia (hence the term, psoriasis rupioides or ostracea). The type of joint involvement found by Falk in his own cases and in the literature on psoriasis arthropathica was variable, usually being a chronic progressive polyarthritis of an

2. Falk, A.: Arch. f. Dermat. u. Syph. **129**:299, 1921.

ankylosing type or a secondary chronic articular rheumatism both gonorrheal and nongonorrheal. Falk is inclined to overlook the distinctive clinical picture of "keratodermie blenorrhagique" as first recorded by Vidal and later by Jeanselme, Chauffard, and other French

Fig. 6.—Detail of infiltrate, showing round epithelioid and mast cells and one typical plasma cell.

authors, the onset, course and spontaneous termination of which is entirely at variance with the chronic course of psoriasis in arthritic subjects. Our own experience has not been in accord with that of Falk. For the past two years we have had under observation at the Cook County Hospital, an unusually severe and extensive case of chronic

deforming arthritis involving practically all the joints of the body. The psoriasis at first involved chiefly the nails, with scattered lesions on the body. Subsequently the eruption became more widespread and involved both palms and soles. The nails, although severely affected, never exfoliated. At one time there were on the palmar surfaces of the fingers and less marked on the feet, small yellow translucent crusts with rounded tops, suggesting in their appearance the crusts of gonorrheal keratoderma. They were not conical and were very small, from 1 to 2 mm. in diameter. These were present a short time and were followed by the ordinary scaly type of lesion. The palmar and plantar lesions were of the ordinary psoriatic appearance, never showing the yellowish brown translucent conical masses which were present in our case of gonorrheal keratosis. We can recall three other cases of psoriasis in arthropathic subjects with involvement of the nails and the usual distribution of psoriasis lesions of the body, but lacking the palmar and plantar involvement and without the exudative tendency noted by Falk.

Adamson's conclusions are conservative, and we cannot but agree that there is a striking resemblance, clinically and histologically, between gonorrheal keratoderma, especially in the generalized cases with lesions scattered over the body, and some cases of arthropathic psoriasis. The resemblance is, however, no closer than that between certain cases of seborrheic dermatitis and psoriasis, and we cannot bring ourselves to believe that gonorrheal keratoderma is a form of psoriasis. The course of keratoderma is markedly characteristic. The lesions involute spontaneously in a few weeks or months, along with the subsidence of the gonorrheal infection. In most cases they never recur, and when they do recur with subsequent attacks of gonorrhea, as noted by Jacquet, they never become chronic but manifest the same tendency to be self-limited. The course of gonorrheal keratoderma alone, disregarding the unique type of eruption, is sufficiently characteristic in our opinion to overbalance all that may be said in favor of its identity with psoriasis. We agree with Adamson that a histologic differentiation is difficult or impossible, and that in generalized cases of keratoderma, such as ours, the lesions on the trunk, scalp and knees suggest psoriasis by their distribution. In view of the fact that of the fifty or more cases of gonorrheal keratoderma reported in the literature, four-fifths were of the localized type confined to the palms and soles, and only one-fifth of the patients had a generalized eruption, further observation and study of these lesions is indicated. The demonstration of the gonococcus in the lesions, which we were unable to demonstrate in our case, would be the deciding factor, unless we accept Jeanselme's theory of trophic disturbance, a gonotoxin affecting the spinal cord. Chauffard believes in a local infectious cause. He found that the serum from the lesions

transferred to the normal skin of the same patient produced a typical new keratosis in two weeks. This special disposition of the skin he calls a "terrain keratosique."

CONCLUSIONS

Our own observations in a case of gonorrheal keratoderma accompanied by generalized eruption incline us to support the early contention of Vidal, Jeanselme, Chauffard and other French writers, that the hyperkeratotic exanthem occurring in the course of severe gonorrheal arthritis is characteristic and peculiar to gonococcal infection and is an affection distinct from arthropathic psoriasis.

NOTE.—Since the observation of this case, a second case of gonorrheal keratosis has been observed by one of us. A young man, aged 32, seen through the courtesy of Dr. F. S. Cary, developed a keratotic eruption ten days after the onset of a multiple gonorrheal arthritis. The skin lesions had been present for two months when seen by us. Their distribution and character were remarkably similar to those in our first case. In addition to the plantar involvement, there were numerous conical waxy papules about the malleoli, knees, hands, forearms and forehead. There were also nail changes and a circinate balanitis. There was the same superficial resemblance to psoriasis, but the conical shape and waxy translucence were different from ordinary psoriatic lesions.

XXIX.—MELANOMA OF THE LOWER LIP

REPORT OF A CASE *

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Resident Physician Barnard Free Skin and Cancer Hospital
ST. LOUIS

REPORT OF CASE

History.—G. C., a girl, aged 2, was admitted on Aug. 7, 1922, to the Barnard Free Skin and Cancer Hospital, in the service of Drs. Engman and Mook. The patient was the elder of two children and had never been sick until the onset of the present illness. The mother said that the birth was that of a normal labor and that the child was breast fed in early infancy.

The mother and father were living and well. One other child in the family, 6 months of age, was living and well. The mother had an aunt who had "cancer of the rectum;" otherwise, the family history was negative.

When the patient was 6 months of age, the mother noticed a "small lump" on the lower lip. It was located just below the vermilion border and to the left of the midline. It was definitely localized and was the size of a large bean. There were no subjective symptoms nor was there any evidence of an inflammatory process. There was no history of trauma. The tumor gradually increased in size, and in eight months it was the size of an average "marble." The mother had consulted several physicians and was advised to have the growth removed. This she refused, and the baby was treated with roentgen rays. Ten minute exposures were given on alternating days, fifteen exposures in all. The setting of the machine, distance and filterage, if any, have not been ascertained. A diagnosis was not made at this time. Following the roentgen-ray therapy, the growth enlarged rapidly and soon ulcerated; the cervical lymph glands soon became visible, and the condition of the patient became steadily worse. The parents then consulted a quack who sold them a bottle of 'radium' to paint the lip with. The case came to this clinic in the deplorable condition shown in Figure 1.

Condition on Admission.—The baby was fretful and poorly nourished, but the cachexia was not so marked as one would expect in the case of an extensive lesion of ten months' duration. The child was unable to sit alone and took nourishment poorly. The temperature was 99 F.; the pulse rate, 136; respiration, 36. The chest examination was unsatisfactory. The abdomen was negative, the reflexes were normal, and the axillary glands were palpable. The neck, the lower half of the face, and the lower lip were markedly swollen. The lower lip was at least three times its normal size, very hard and presented a large, irregular ulceration extending downward and to the left. Near the periphery of the ulcer there were a few pearly nodules. The mouth could not be opened very widely. The lower anterior teeth were covered with the growth. The infiltration of the neck was extensive, smooth, boardlike and

* Studies, reports and observations from the dermatological departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

extended posteriorly to each mastoid process. Figure 1 shows the extent of the infiltration, and the folds in the supraclavicular regions. The glands in the supraclavicular spaces were distinctly palpable.

Laboratory Findings.—These were: Wassermann test, negative; white blood cells, 9,000; red blood cells, 4,576,000; hemoglobin, 70 per cent.; lymphocytes, 37 per cent.; large mononuclears and transitionals, 7.6 per cent.; polymorphonuclear neutrophils, 52.8 per cent.; and unclassified cells, 2.6 per cent.

Tentative Diagnosis.—Sarcoma with a possibility of carcinoma was the tentative diagnosis.

Histologic Findings.—On Aug. 9, 1922, a biopsy was performed under local anesthesia. A rectangular section, 1 by 1.5 cm., was removed from the lower left angle of the chin, including the rolled border of the ulcer and some

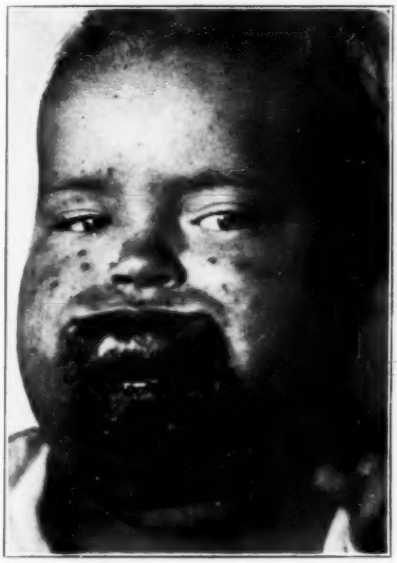

Fig. 1.—Melanoma of lip; condition on admission.

normal skin. The sections were stained with hematoxylin and eosin, polychrome-methylene blue and acid orcein.

The tumor was composed of small round cells with relatively little cytoplasm and sharply staining vesicular nuclei. These cells were laid in and were loosely attached to a well organized stroma. The stroma was composed of narrow densely fibrous columns surrounding alveolar-like spaces. Some lined these spaces; in others, they filled them. A section taken through the skin of the lip showed that the whole of the true skin and of the subcutaneous tissue were involved. The epithelial layer was apparently pushed up in places, but there was no evidence of increased growth in this layer nor evidence that the tumor arose from it. On the other hand, it was atrophic in many places.

Clinically, the tumor was either a sarcoma or a melanoma. The metastases were characteristic. Histologically, the cells appeared in many places to

behave more like epithelial cells than cells of connective tissue origin. The tumor resembled in many ways certain rare types which have been seen to arise from the hypophysis and the tail of the pancreas.

An abstract of the history and pathologic sections were submitted to Dr. James Ewing, his report was partially as follows:

"Your tumor of the child's lip is a melanoma. I feel reasonably sure of this diagnosis from the clinical history. No other tumor goes through the body like wildfire as this one did. The sections confirm the clinical impression. The only thing lacking is pigment, but this makes no difference since many of the worst of these tumors lack pigment. Then there may be traces of pigment lurking about, which I can't find. The cell groups are characteristic in many places, not in all. More eosin would make them appear opaque as does the polychrome."

Fig. 2.—Melanoma of lip; condition six weeks after radium treatment.

Clinical Course.—The prognosis was considered hopeless, but palliative measures were undertaken. Radiation was the only method that might be of value. The whole area, including the lip and the glands in the supraclavicular regions, was divided into areas 4 by 2 cm., and each area was exposed once to radiation for five hours from 100 mg. of radium filtered through 5 mm. of silver, 2 mm. of brass, and 1 mm. of rubber at a distance of 2 cm. Within a week, seventeen areas were treated. There was rapid reduction in the infiltration, with marked improvement in the general condition of the patient. The child's appetite improved, and she was soon able to play about the ward of the hospital. No severe constitutional symptoms followed the radium therapy.

On Sept. 4, 1922, a small freely movable lump about the size of a walnut was noticed in the upper third lateral aspect of the right thigh. This was given two treatments with radium as outlined above, with resultant marked

Fig. 3.—Photomicrograph of section of melanoma of lip (low magnification).

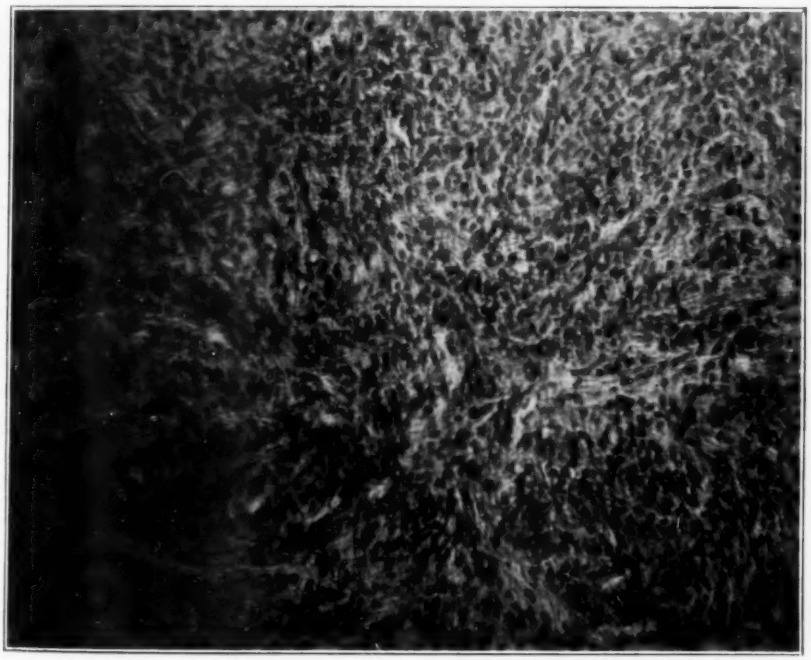

Fig. 4.—Photomicrograph of section of melanoma of lip showing type of cells (high magnification).

reduction in size. At this time a radiographic examination of the chest and thighs was requested as the result of which the following report was made by Dr. Edwin C. Ernst:

"The radiographic examination of the chest shows an increase of thickening in the hilar and peribronchial regions and quite an enlargement of the cardiac shadow, especially toward the left side. The upper end of the shaft of each femur shows apparently a rarefaction and also an increase in diameter in this region along the margins suggesting possible tumor pathology (probably metastatic)."

On September 14, the blood findings were: red blood cells, 4,192,000; white blood cells, 2,500; hemoglobin, 65 per cent.; lymphocytes, 26 per cent.; large mononuclears, 18 per cent., and polymorphonuclear neutrophils, 56 per cent.

On September 20, the patient refused to walk and seemed to protect the right leg, especially against weight bearing. Palpation of the growth elicited pain.

On September 27, the mother was called home on account of illness of the younger child. At this time, the patient was unable to walk. There was considerable pallor and weakness, but the child was bright and took nourishment well. The mother was advised to return in a month. Figure 2 shows the condition at this time.

October 24, 1922: On readmission to the hospital, there was marked wasting; the breathing was difficult and numerous râles were heard at the base of each lung posteriorly. Small subcutaneous nodules were present on the right forearm and on each thigh. In the suprasternal notch, there was a growth as large as a pigeon's egg. The right side of the face and neck were enlarged as much as when the child was first admitted to the hospital. The mother was advised to return home as it was impossible to offer any encouragement.

SUMMARY

1. A case of melanoma of the lower lip occurring at a very early age is reported.

2. Although histologically the tumor was a melanoma, clinically it could not be differentiated from sarcoma. The lip is not a common site of the origin for sarcoma,[1] only a few cases being on record.[2]

3. The rapidity of growth following roentgen-ray therapy is characteristic of melanoma, although Montgomery and Culver[3] have reported a case of melanoma of the lip in which favorable results followed radium therapy.

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1. Markley, A. J.: Primary Sarcoma of the Lower Lip, J. A. M. A. **61**:334 (Aug. 2) 1913.

2. Sweitzer, S. E., and Michelson, H. E.: Primary Sarcoma of the Upper Lip; Report of a Case, J. A. M. A. **77**:1563 (Nov. 12) 1921.

3. Montgomery, Douglass W., and Culver, George D.: A Melanotic Tumor of the Lip Treated with Radium, Arch. Dermat. & Syph. **2**:5 (July) 1920.

FURTHER CONTRIBUTIONS TO THE EXPERIMENTAL ASPECTS OF IODID AND BROMID EXANTHEMS*

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ANN ARBOR, MICH.

In May, 1922, my associates and I presented before the American Dermatological Association the results of a preliminary study on the experimental aspects of iodid and bromid exanthems. In the preliminary report [1] it was shown that the ingestion of bromid readily displaced the chlorid in the blood; that apparently the kidney, readily filtering through both chlorid and iodid, reacted differently to the salts of bromin. These tend to be stored up after their ingestion, owing to the difficulty of their filtrability through the kidney epithelium. The constant ingestion and gradual storing up in the body of bromid (small amounts being eliminated through the bowel) leads to the clinical phenomena known as bromism.

The most striking manifestations of bromism are its effects on the central nervous system and on the skin. It was shown in our previous communication that no trace of bromid can be found in the local lesions of bromoderma, except possibly when these are contaminated by the circulating blood. It was further determined that there is apparently no relation between the amount of bromid ingested and the appearance of exanthems.

In the discussion which followed the presentation of our preliminary studies, we brought out that it seemed quite likely that stored-up bromids could be pushed out of the body, so to speak, by mass action of relatively large amounts of chlorid; that is to say, that the initial process of displacement of chlorid by bromid could be reversed. We based our belief at that time on our experience in treating a patient with bromoderma with intravenous injections of sodium chlorid solution. We were able to state at that time that, thus treated, bromid was apparently liberated in the urine, with the almost immediate clearing of the mental symptoms and a marked amelioration of the cutaneous ones.

During the past three months I have had the unusual opportunity of studying, over a relatively long period of time, three cases of bromism, in all of which mental symptoms were present, together

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* From the University of Michigan Medical School.

* Studies and contributions of the Department of Dermatology and Syphilology of the University of Michigan, service of Dr. Udo J. Wile.

1. Wile, U. J.; Wright, C. S., and Smith, N. R.: A Preliminary Study of the Experimental Aspects of Iodid and Bromid Exanthems, Arch. Dermat. & Syph. **6**:529 (Nov.) 1922.

with typical nodular bromid lesions of the skin. These cases have responded in so remarkable a manner, and by a study of the urinary findings have in so interesting a fashion justified our preliminary conclusions, that they are herewith reported.

REPORT OF CASES

Case 1.—A woman, about 40 years of age, was admitted to the Hospital on Oct. 31, 1922, complaining of "sores" on the legs, and "nervousness." Her "nervousness" had been present for the past ten years. She had been taking bromids in small amounts during the past four years. Ten weeks previous to admission, owing to an especially bad upset due to domestic difficulties, she was particularly "nervous," and took large amounts of bromids; the exact dose was not known. The eruption began on her legs as small pea-sized, painful, pruritic pustules, which rapidly increased in size during the ten weeks of their presence. For two weeks previous to her admission she had been incoherent and extremely excitable. Cutaneous examination revealed a large number of various sized nodular lesions, typically warty and grayish brown, and entirely characteristic of a nodular bromoderma. The lesions were limited to the lower extremities. Her mental condition suggested a "toxic encephalitis," occurring in a patient who has been a constitutional psychopath for many years. During her stay, she became violent at times, and was, until treatment began, entirely irrational.

The patient entered the hospital on a stretcher, and as an emergency case. She was confused and incoherent. She was immediately given 500 c.c. of decinormal saline solution intravenously. Almost immediately, she developed a severe chill. The temperature rose to 103 F., the pulse rate to 140; and she became stuporous, had cyanosis, and at times was almost pulseless. A preliminary examination of the urine had shown it to be practically normal and to contain no bromid. The morning following the injection, she was catheterized, and the urine showed enormous amounts of albumin and many casts. The test for bromid was strongly positive. The patient rapidly recovered from the apparent condition of the shock into which she was thrown by the injection, and her mental condition was considerably clearer. Her temperature dropped to normal within the next forty-eight hours, and the nephritis cleared up in the next two or three days, with decreasing amounts of albumin and casts, and a corresponding decrease in the positive test for bromin.

Owing to the marked shock which the patient experienced, further treatment was not carried out until ten days later, and during this period she relapsed mentally, again becoming violent and having delusions of persecution. The bromoderma, however, showed a continuous and marked improvement.

On November 16, two weeks following her admission, the patient received 100 c.c. of decinormal saline solution intravenously. About twelve hours later she became normal, was able to converse intelligently, and remained rational until eight o'clock the following night. The following day she again cleared mentally and remained so until the time of her discharge from the hospital.

Within a few hours following the second injection, the urine of the patient was found to contain a small amount of albumin and large amounts of bromid.

Bromin in the urine was detected readily in this as in the remaining two cases by the addition to 10 c.c. of twenty-four hour specimen the urine of a few crystals of potassium permanganate, and then of about 0.5 to 1 c.c. of concentrated sulphuric acid. The urine of this patient thus treated showed the

presence of bromin, which could readily be detected by its strong odor, as well as by a distinct, although small amount of bromin vapor, which was liberated.

This patient received, during her two weeks' stay, two more injections of saline solution, one of 100 c.c. and one of 200 c.c. These were followed by continuous improvement in the local lesions, and were tolerated without any reaction or any signs of renal irritation. The patient was discharged from the hospital on Dec. 1, 1922, in apparently good health, both as to her mental and to her skin condition.

Case 2.—This patient was referred to me from the psychiatric service of Dr. A. M. Barrett, on Jan. 19, 1923, for a diagnosis of an eruption over the body. The patient was a Roumanian, and a history of her mental difficulty was not obtainable from her. She had been admitted to the psychiatric hospital for some mental condition, the diagnosis of which was later established as paranoia. The patient was able to state, however, that she had been taking "Orangeine" powders and "Bromo-Seltzer," together with medicine which had been given to her by her home physician for "nervousness' and insomnia.

On examination, this patient was found to have an extensive nodular bromid eruption, the lesions being more extensive than in the first case, being present not only on the legs, but on the back as well. A preliminary examination of the patient's urine disclosed no bromid. On January 27, she received 250 c.c. of decinormal sodium chlorid, from which she suffered no reaction, but there was an almost immediate improvement in her mental condition. She was brighter at this time, and responded intelligently to questions. A specimen of urine following this treatment gave nothing more than a suggestion of bromid. On January 30, three days later, she received 300 c.c. of decinormal saline solution. At this time her urine contained a definite trace of bromid. Further treatment was not carried out, owing to the patient's refusal to cooperate. Marked improvement, however, was noted in the cutaneous manifestations, as in the first case. A few days following the second injection the lesions had almost entirely involuted.

Case 3.—This patient entered the hospital on Feb. 9, 1923, and is still in our wards. She was 29 years of age, and came to the hospital on account of a painful eruption over the legs and arms, and "nervousness."

Examination revealed a most extensive "erythema nodosum" over the entire body, for the most part, however, on the extremities. Together with this, she had a distinct, painful "polyarthritis," with characteristic fever and sweats. Scattered on both legs, and independent of the lesions of erythema nodosum, were numerous lesions of a deep nodular and pustular bromid exanthem. The patient volunteered the information that every night since November, 1922, that is, three months previous to her admission, she had been taking a "salty medicine" to induce sleep. She was immediately placed on treatment for erythema nodosum with salicylates, and soon improvement was noted. It was also noted that the patient's mental reaction was slow, and a description from the psychiatric department stated that she presented a "toxic mental state, probably dependent on a bromism."

Examination of the patient's urine, made previous to the treatment directed toward the bromism, revealed, as might be expected from her severe infection with rheumatic fever, the presence of albumin. A positive test for bromin could not be elicited. On February 15, she received 300 c.c. of decinormal saline solution. The test of the first twenty-four hour urine was negative for bromin. On February 19, four days later, she received 400 c.c. of decinormal

saline solution. A trace of albumin was present in the urine, and a strongly positive test for bromin. Almost immediately following the first injection of sodium chlorid solution, the bromid lesions showed marked regression. Within a few days, however, there was a marked accentuation, not only of the local lesions, but it was also observed that many new lesions appeared. Subsequent injections resulted, for about a week, in several new groups of bromid lesions. After this period, all the lesions began to regress, and finally, after five injections, all had completely disappeared.

COMMENT

1. Three patients, all women, suffering from mental and cutaneous manifestations of bromism, were markedly benefited, both with regard to the mental state and to the cutaneous condition, by the intravenous administration of decinormal salt solution given at two or three day intervals.

2. In all three cases, bromin could not be determined in the urine previous to the administration of the salt solution. The prompt appearance of the bromin—in two cases following the first injection, in the third following the second—leads to the conclusion that the mass action of the chlorid had thrown bromid out into the blood, relieving the apparent mental toxemia, and in a similar fashion causing a marked diminution and gradual disappearance of the cutaneous manifestations.

3. The sharp nephritis, together with symptoms of actual shock, in the first case, can be explained probably by the sudden chemical change taking place in the tissues. The irritating effect of the passage of a bromin salt through the renal epithelium adds weight to the theory before mentioned, that bromid does not readily filter through the renal epithelium. Further weight is added to this view by the prompt disappearance of the nephritis coincident with the disappearance of the bromid in the urine.

4. Intravenous injection of normal salt solution is advocated in the treatment of both cutaneous and mental symptoms of "bromism."

CARBON TETRACHLORID IN DERMATOLOGY

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SAN FRANCISCO

Jacquemet and Goubeau's article [1] on the therapeutic uses of carbon tetrachlorid in cutaneous medicine first called my attention to its possibilities. For the past two years I have been using it as an external application, with satisfactory results. It is inexpensive, and when used with full knowledge of its possible depressing effects, is a comparatively safe remedy.

Carbon tetrachlorid, or tetrachlormethane, is obtained from carbon disulphid and chlorine gas by heat ($C Cl_4$). Thorpe [2] discusses its chemistry. According to Jacquemet and Goubeau,[1] it is "a colorless liquid of a density of 1.6 with an agreeable odor (when pure) similar to chloroform ($C HCl_3$). It is a solvent of iodin, camphor, rubber, greases, and essential oils. It is miscible with alcohol, benzol, and petrol. . . . It has anaesthetic properties."

Its successful internal use is noted in the treatment of uncinariasis in which as much as 3 c.c. have been given internally in capsules, by Hall,[3] Leach,[4] Nicholls and Hampton,[5] and McVail.[6] Larger doses internally have had a soporific action [3] and gave other indications of being depressing. As early as 1867, its action as a general anesthetic was discussed by Sansom [7] and Nunneley,[8] and its depressant effects emphasized. Docherty, and Burgess [9] quote animal experiments and human necropsies in which it was observed that degenerative changes were produced in the liver and kidneys. They state that a dose of 5 c.c. seems "on the border of the danger line," and "the safe maximum

1. Jacquemet (of Grenoble) and Goubeau: Bull. gén. de thérap. **171**:268, 1920-1921.

2. Thorpe: Dictionary of Applied Chemistry, New York, Longmans, Greene & Co., **1**:671,1912.

3. Hall, Maurice C.: The Use of Carbon Tetrachlorid for the Removal of Hookworms, J. A. M. A. **77**:1641 (Nov. 19) 1921.

4. Leach, C. N.: Carbon Tetrachlorid in the Treatment of Hookworm Disease, J. A. M. A. **78**:1789 (June 10) 1922.

5. Nicholls and Hampton: Brit. M. J. **2**:8 (July 1) 1922.

6. McVail: Indian M. Gaz. **57**:290 (Aug.) 1922.

7. Sansom: Brit. M. J. **2**:206 (Sept. 7) 1867.

8. Nunneley: Brit. M. J. **1**:685 (June 15) 1867.

9. Docherty and Burgess: Brit. M. J. **2**:907 (Nov. 11) 1922.

dose seems to be 3 c.c." All who have written on the subject agree that the drug, administered internally, seems to be a specific for ankylostomes and fairly efficient in the removal of various other intestinal parasites. All agree, furthermore, that an overdose of the drug may produce untoward and severe symptoms. A fatality resulting from inhalation of a large amount of the fumes during a carbon tetrachlorid shampoo is recorded in the London letter in *The Journal of the American Medical Association.*[10] Necropsy revealed the existence of status lymphaticus. Other cases of collapse from inhalation of the fumes are mentioned in the letter. It is stated, however, that this fatality was the only one after 30,000 shampoos with the preparation. Inhalation of very much of it will produce dizziness, so its depressant action must not be forgotten in prescribing it in more than small amounts for external use.

My attention was called to the possible external uses of the drug in dermatology by the pioneer work of Jacquemet and Goubeau.[1] They discovered that it was very useful in various seborrheal conditions and infections of the skin. I have been able to duplicate these results at Stanford and have made other observations which are presented herewith.

A few others have recorded their experiences with tetrachlormethane. Foster [11] found that it was an efficient delousing agent when applied to infested clothing. Twenty-five cubic centimeters of tetrachlormethane were placed on filter paper on top of a complete outfit of a soldier's folded clothing in a closed can with a small opening at the top for the exit of air. The vapor percolated through the clothing, and after two hours all of the lice and nits were found dead. The heavy vapor given off by the drug was found to be toxic also for flies, ants and potato bugs.

Wederhake [12] discusses its uses as a noninflammable penetrating vehicle for various antiseptics useful in surgery. For these purposes it can replace the highly inflammable ether or benzene. He uses the following formula for disinfection of the hands and in preparing the skin for operation:

	Gm. or C.c.
Iodin, pure	1|0
Paraffin, solid (43 degrees)	0|5
Tetrachlormethane	100|0

This is applied after five minutes' preliminary washing with a brush or rough cloth without soap. After operation, the hands are

10. A Fatal Shampoo, London Letter, J. A. M. A. **53**:392 (July 31) 1909.
11. Foster: Pub. Health Rep. **33**:1823 (Oct. 25) 1918.
12. Wederhake: Deutsch. med. Wchnschr. **33**:596, 1907.

cleaned with a cloth soaked in tetrachlormethane. Instead of paraffin, India rubber may be used. Of course, the preparation should be chemically pure.

MacAuliffe[13] discusses its great value as an inexpensive antiseptic cleansing agent in the treatment of "war wounds." He found that 1 liter would cleanse "more than three hundred wounds effectively."

Jacquemet (of Grenoble) and Goubeau[14] first called attention to the various uses and value of carbon tetrachlorid in dermatology. They used a "double rectified" preparation. The commercial product contains chlorin or sulphur, has a disagreeable odor, and is very irritating to the skin. It is recommended that it be kept in brown glass bottles, away from the light. A piece of chalk the size of a nut should be placed in a bag of gauze in the bottle containing 1 liter. Traces of sulphur will be carried down by the chalk as calcium sulphid. Unpleasant results are avoided if a pure double rectified preparation is used. It was found that the preparation is a good antiseptic, and that this quality is greatly aided through its strong affinity for fatty substances. It penetrates deeply into the sebaceous gland ducts and hair follicles, dissolving sebaceous material. Various other antiseptics are readily soluble in it, for instance, iodin, bromin, camphor and many of the essential oils. A 3 per cent. solution of iodin in tetrachlormethane makes a useful penetrating, antiseptic solution.

As a parasiticide, it is effective, killing pediculi and many other insects instantly. Its greatest use is found in the local treatment of various seborrheal conditions. In a later article[15] Goubeau refers to Jacquemet's and his own experiences and observations extending over three years. He also gives references to their previous publications on the subject.[16] He states that tetrachlormethane has proved to be useful in various forms of "acne, folliculitis, psoriasis, and the mycoses." It is recommended in "all cases where deep disinfection of the skin and the cul de sacs of the glands is necessary. . . . It will clean a seborrhoeic skin of grease or cause the recuperation of a dry skin by the application of fatty substances dissolved in it." Goubeau reports in detail the successful treatment of two severe rebellious cases of seborrheic eczema, one of seven years' and the other of five years' duration. Both patients responded completely within a few weeks and have remained well. There was no internal medication in the first case, but iodin was given in the second case on

13. MacAuliffe: Bull. de l' Acad. de méd. **76**:180, 1916.

14. Footnotes 1 and 10.

15. Goubeau: Bull. Soc. franç. de dermat. et syph. No. 6, p. 295 (May 18) 1921.

16. Jacquemet: Dauphiné méd., June, 1909; May, 1913.

account of hyperthyroidism. The local treatment in both cases was as follows: At night the affected areas were compressed with cotton saturated with the following solution:

	Gm. or C.c.
Carbon tetrachlorid (twice rectified)	125
Wool fat to saturation	
Balsam of Peru	2
Oil of lavender	1

After the evaporation of the C Cl_4, the following salve was applied.

	Gm. or C.c.
Wool fat	40|0
Balsam of Peru	1|0
Oil of birch	4|0
Essence of bergamot	1 drop

The next morning the areas were cleansed with pure tetrachlormethane in cotton. This was the daily routine. A few obstinate places showing a tendency to spread were promptly controlled by application of 2 per cent. camphor in carbon tetrachlorid. These two successfully treated cases were cited as examples, of which a large number had been observed. The author warns against using an impure preparation as it is irritating and has a very bad odor. He also states that one should be extremely careful to avoid inhaling much because it will produce vertigo, headache and dyspnea. Darier, in his discussion of the paper, endorses these observations.

I have used chemically pure carbon tetrachlorid extensively during the past two years. In addition to all the advantages claimed by Jacquemet and Goubeau, it fills an important place in the armamentarium of surgeons and dermatologists in regions in which alcohol is difficult or impossible to obtain. In my practice I use a great deal of alcohol locally. Frequently patients find that they cannot have their prescriptions calling for alcohol filled. Carbon tetrachlorid may partially solve their problem.

Dermatologists find fat solvents a necessity in their practice. The usual solvents—ether, benzene and chloroform—are highly inflammable and therefore dangerous. So carbon tetrachlorid, an efficient fire extinguisher, again qualifies as a useful agent. Furthermore, this substance is inexpensive. Possibly the cost may ascend rapidly when wholesalers note an increased demand. At present the chemically pure product sells wholesale here at 50 cents a pound, or $3 a gallon.

I have discovered few new uses, but expect soon to be able to publish a report on the histologic changes produced in the skin by the drug. Jacquemet and Goubeau have observed that it produces no pathologic effects on the skin if a double rectified preparation is used. I have had the experience of seeing the skin on the cheeks (where the

epidermis is thin normally) badly burned by an impure preparation dispensed by a careless pharmacist. The cauterized areas healed extremely slowly.

The pure drug is a good cleanser, penetrating gland ducts and hair follicles readily. In seborrheal conditions in which keratolytic action is desired, I frequently use the following for this purpose:

	Gm. or C.c.
Salicylic acid	3|0
Oil of rose geranium q. s.	
Carbon tetrachlorid (chemically pure)..	100|0

If the skin is dry, wool fat (10 or 20 per cent.) is added. In the preliminary keratolytic treatment of psoriasis, seborrheic eczema, or similar conditions, the same lotion with hydrous wool fat and an increased amount of salicylic acid is used. The weaker cleansing lotion, followed by lotio alba, often is useful in acne vulgaris. Sometimes the replacement of half the rose water in lotio alba with tetrachlormethane has a good effect. The latter does not go into solution with aqueous preparations, but this does not interfere greatly with its local action in acne. The addition of resorcin (2 per cent.), or phenol (1 per cent.) or camphor (5 per cent.), or all three combined will rapidly cleanse and sterilize various pyogenic infections, if they are not very extensive. Paraffin can be melted and incorporated with carbon tetrachlorid and other soluble ingredients if water or alcohol is not present in excess. Salicylic acid, when dissolved in ether, alcohol or chloroform, is miscible with tetrachlormethane.

Further experimentation will develop new uses for the drug and, in my opinion, it will prove to be one of the most effective external therapeutic agents in dermatology.

So far, we know that it has these valuable properties: (1) bactericidal; (2) insecticidal; (3) solvent of fats and débris in ducts and follicles of the skin; (4) penetrating vehicle for medicaments to be carried into the skin, and (5) rapidly drying skin cleanser.

240 Stockton Street.

COLLOID ACNE

IS COLLOID ACNE A FORM OF COLLOID MILIUM?*

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PHILADELPHIA

Under the term "acne colloidienne," Brocq[1] describes a "rare variety of acne in which the lesions are scattered here and there in an irregular manner upon the cheeks but which is characterized by the fact that the perifollicular tissues, the site of the lesions, become light yellow, transparent, colloid-like in aspect. These lesions are secondary to acneic eruptions, which fact, together with their peculiar distribution, differentiates them from colloid milium. Their resemblance to disseminated lupus vulgaris is extremely close and their relationship to this latter very difficult to decide. In certain respects they resemble the tuberculides."

A study of the literature reveals no further reference to colloid acne.

REPORT OF CASES

CASE 1.—R. N., a woman, white, blonde, aged 18, had had acne vulgaris for five years.

When first observed, this patient presented seven colloid lesions scattered here and there on the face. They were accompanied by new and disappearing acne lesions which presented the usual phenomena of acne. The spots that looked colloid-like were light yellow, flat, perifollicular, soft and nonresistant; when punctured with a fine cataract knife they gave exactly the same sensation given by lupomas when similarly punctured. On expression, a small amount of a jellylike material was obtained; this was followed by a drop or two of blood. The patient remarked that some of the marks subsequent to the resolution of active acne lesions remained for a much longer time than the majority of them. Evacuation was followed by usual cicatrization.

CASE 2.—M. C., a woman, aged 19, white, blonde, had had acne vulgaris for seven years. When first observed, this patient presented six colloid lesions and the general phenomena common to ordinary acne vulgaris. During the course of treatment, two additional lesions made their appearance.

CASE 3.—A. M., a woman, aged 19, white, a brunette, had had acne vulgaris for five years. When first observed, this patient presented four colloid lesions. The same general phenomena as in the other patients were present.

CASE 4.—M. K., a man, aged 23, white, a brunette, had had acne vulgaris for eleven years. When first observed, this patient presented four colloid lesions. Two of these lesions were located over the angle of the right jaw

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1. Précis-Atlas de pratique dermatologique, Paris, Doin, 1921, p. 1126.

and were unquestionably similar to the lesions under discussion. They gave the jellylike material on puncture and expression. The other two lesions were on the lower right side of the nape of the neck. One of these was removed for histologic study but simply showed the usual changes of circumscribed post-suppurative resolving lesions.

SYMPTOMATOLOGY

Colloid acne occurs in patients with acne vulgaris and usually upon the face—the site of acne exposed to the inclemencies of the weather. Patients usually notice that whereas the macules left by most receding acne lesions disappear, certain of these spots do not disappear with as equal a rapidity—as a rule, not for months. The lesions are pinhead or slightly larger in size, are flat as if encased in the skin, although occasionally they are slightly elevated; they are perifollicular, well defined and circumscribed, reddish-yellow to yellow; this color is particularly defined on diascopy, and when observed in this manner the lesions hardly differ from the apple-jelly like appearance of the lupic tubercle.

The number of lesions is generally small, up to ten would probably give the maximum limit. Two lesions may be close enough to coalesce, but the same characteristics are maintained. They are limited to the exposed surfaces of acne sites—notably the face. The type of complexion does not appear to be a factor, as two of our patients were dark and two were light.

The lesions appear during the course of pustular acne, most commonly—in our cases at least—of the superficial type, and may maintain the same appearance for months. When punctured, the lesion gives one the sensation of being extraordinarily soft, and when a comedone extractor is applied, a jellylike material is expressed. This maneuver is followed by the appearance of one or more droplets of blood. Subsequently, the ordinary acne cicatrix develops, although in some instances there is a redevelopment of the original condition, requiring similar treatment for removal. It appears that these lesions do eventually cicatrize in a normal manner; however, cicatrization can be hastened by mechanical evacuation. The new granulations ought to be subsequently protected from irritation by means of suitable applications.

The reddish color is most marked in the earlier stages and is probably due to the same factors present in all granulation processes. In the fully formed lesion, most of the reddish tint is absent and the clear yellow tint described by Brocq is evident. In some instances it seems that the yellow stage is transitory and is rapidly replaced by the ordinary cicatrix. This would indicate that transient lesions occur, but, as has already been remarked, progress toward cicatrization, in the majority of instances, is slow. It might be noted here that in the

stage when the reddish tint is most marked there is no clinical difference from what is ordinarily seen in an acne lesion progressing to cicatrization. This is likewise a histologic fact and no doubt explains the histologic picture of the sections made from the neck lesion of Patient 4.

DISCUSSION AND DIFFERENTIAL DIAGNOSIS

As a part of or following acne eruptions, certain degenerative formations may be observed, namely: Exceedingly large comedones (tannes of the French); butyric acid cysts which result from a further degenerative change in comedones and from which a yellowish smelly fluid may be expressed; mucoid cysts which, according to Sabouraud, are due to cystic degeneration in long obstructed sebaceous glands, from which a mucous or gelatinous matter may be expressed. To these degenerative changes may be added a condition less apparent clinically, unless the skin be closely observed, which often marks the acne patient for months and the lesions of which, like the others, require mechanical measures for their removal. This is colloid acne, and it may be added that at the present time no better clinical term could be selected.

It is generally admitted that when the elastic fibers of the derm are destroyed by rupture, inflammation, or necrosis, return to normal or regeneration does not occur. However, observers have noted that in granulomatous processes and in scars fine elastic fibrils develop. These fine fibrils, no doubt, lack the vitality of normal elastic tissue, and it is possible that under certain conditions they degenerate easily.

Elastic degeneration in granulation tissue, in which distinct clinical changes occur, was first clearly described by Juluisberg,[2] although Jarisch[3] many years before observed the condition in a tertiary syphilid. Kissmeyer and With,[4] who recently made one of the finest contributions to the study of elastic degenerations of the skin, note that elastic degeneration occurs either in the form of a marked increase in the elastic fibers often accompanied by the elastorrhexis of Darier or in the form of amorphous strongly staining lumps or grains. Owing to the special site of colloid acne lesions, we were, unfortunately, unable to obtain proper histologic material. Nevertheless, it is not improbable to suppose that colloid acne is, partially at least, an expression of elastic degeneration occurring in some of the granulomatous lesions of acne.

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2. Juluisberg, Fritz: Ueber colloide degeneration der Haute speciell in Granulations und Narbengewebe, Arch. Dermat. u. Syph. **61**:175, 1902.

3. Jarisch: Colloidoma ulcerosum, Verhandl. d. v. Cong. Deutsch. Dermat. gesellsch., 1896 (Case demonstration).

4. Kissmeyer, A., and With, C.: Clinical and Histological Studies on the Pathological Changes in the Elastic Tissues of the Skin, Brit. J. Dermat. & Syph. **34**:175 (June) 1922.

If this supposition is correct, colloid acne may be classed with Kissmeyer and With's group of presenile degenerations of newly formed elastic tissue of granulomatous processes. As the lesions of colloid acne occur on parts not protected from climatic conditions, it is quite likely, as they suggest, that the weather factors may be held responsible for the degeneration of these newly formed, poorly resistant elastic fibrils.

I have not noted these lesions in already formed scars of acne, although elastomas have been observed in scars resulting from other diseases, notably variola. It appears that colloid acne occurs only in the granulomatous stages, that is, before a well-formed scar has developed.

Since histologic studies have not been made in colloid acne, still another explanation is possible. Pustular acne lesions, which have not ruptured, gradually flatten as absorption occurs, but some of the pus, failing of absorption, changes into the jellylike substance obtained on expression.

From the differential diagnosis given by Brocq it is evident that the clinical appearance of these circumscribed lesions is, in itself, not pathognomonic. In the presence of a concomitant acne vulgaris, disseminated lupus vulgaris depends on the history for its diagnosis as well as on its lack of perifollicular situation. Colloid milium must be seriously considered. Both occur in patients past the age of puberty; both occur on the face, rarely elsewhere; both give a jellylike substance on expression, a droplet or two of blood, and are then subsequently replaced by a slightly contracted cicatrix; both claim as theoretical etiologic basis more or less habitual exposure to the weather. Furthermore, it has been definitely shown that the colloid degeneration in colloid milium is particularly marked about the sebaceous glands and hair follicles.[5] In addition, there is a similarity clinically in size, color and consistency.

It is possible, as Juluisberg points out,[2] that at least one of the forms of colloid milium is due to an earlier affection, as, for example, an acne pustule. If this is the case, and clinical studies appear to indicate that this is so, colloid acne is but an aborted form or an early stage of at least a variety of colloid milium. In view of the fact that colloid acne is clearly a secondary manifestation to a well-defined condition, Juliusberg's hypothesis should be seriously considered—that is, that colloid milium represents a secondary manifestation of a preexisting condition, a scar or granulation tissue in which the products of elastic degeneration predominate.

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5. Pusey: Principles and Practice of Dermatology, Ed. 2, New York, D. Appleton & Co., p. 849.

Correspondence

Bullous Lesions in Sarcoma of Kaposi and Lichen Planus

To the Editor:—In our article on "Bullous Lesions in Sarcoma of Kaposi and in Lichen Planus," in the May issue of the ARCHIVES, we said:

"We have not discovered any other record of hemorrhagic sarcoma of Kaposi in which bullous lesions formed a part of the general eruption."

We find that we are in error. Dr. Herman Goldenberg called our attention to the following articles:

Dalla Favera: *Arch. f. Dermat. u. Syph.* **109**:387, 1911. Pick, W.: ibid. **87**:267, 1907.

In these papers lymph-cysts in Kaposi's sarcoma are described.

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Abstracts from Current Literature

ON OCCUPATIONAL SENSITIZATION TO THE CASTOR BEAN. H. S. Bernton, Am. J. M. Sc. **165**:196 (Feb.) 1922.

This is a report of acquired sensitization, in a chemist, to the castor bean, resulting in sneezing and asthma. Cutaneous tests were positive with a 1:250,000 dilution of the protein meal.

THE NATURE OF THE COMPLEMENT FIXATION REACTION IN SYPHILIS IN RELATION TO THE STANDARDIZATION OF TECHNIC. J. A. Kolmer, Am. J. M. Sc. **165**:320 (March) 1923.

Kolmer believes that positive reactions will be obtained only in syphilis and frambesia tropica with the constantly improved technic. For biologic reasons, false negative reactions will continue to occur on account of lowered vitality and the activity of the infecting organism.

The antibody responsible for the reaction is developed by infection with the spirochete of syphilis and frambesia but is probably not a lipoid nor identified with the lipoids of the blood or spinal fluid.

The article concludes with the requirements for improved technic by standardization and are discussed at length in previous writings.

SOME OBSERVATIONS UPON THE HISTOLOGICAL CHANGES IN LYMPHATIC GLANDS FOLLOWING EXPOSURES TO RADIUM. J. C. Mottram, Am. J. M. Sc. **165**:469 (April) 1923.

The conclusions drawn from this work are, briefly: The lymphocytes, entering the gland by afferent lymphatics, are devoured by endothelial cells which gradually change into follicle cells. Cell division occurs, and follicle cells are converted into plasmocytes or myelocytes, these in turn dividing into lymphocytes which leave the gland by efferent lymphocytes or by the blood vessels.

DISFIGURING SCARS—PREVENTION AND TREATMENT. J. W. Bransfield, Am. J. M. Sc. **165**:562 (April) 1923.

This article deals with surgical treatment and repair of old depressed scars. The author recommends the use of mattress sutures and a coaptation button, producing overcorrection of the deformity and skin edge eversion which subsequently contracts, leaving a soft normal scar.

AN UNUSUAL TYPE OF NODULAR LEPROSY IN THE SUDAN. R. G. Archibald, Ann. Trop. M. & Parasitol. **16**:34 (Dec. 30) 1922.

In the case described the patient presented lesions which could have been confused with syphilis, molluscum contagiosum, yaws, prurigo, cutaneous Leishmaniasis and lichen hyperkeratosis. The lesions were small, round, firm, shotty papules, generally distributed, some being slightly inflammatory at the base. As the patient became worse under antisyphilitic treatment, a papule was excised, and the lymphatics were found to be filled with lepra bacilli. This is spoken of as a possible miliary type of leprosy.

THE OCCURRENCE OF THE LARVAE OF ONCHOCERCA VOLVULUS (LEUCKART 1893) IN THE SKIN OF NATIVES OF THE GOLD COAST. J. F. Corson, Ann. Trop. M. & Parasitol. **16**:407 (Dec. 30) 1922.

Many natives had larvae of this parasite in their skins, especially if there were also present the tumors of *Onchocerca*. There was, however, no proved relationship between the larvae and the cutaneous conditions present in some of the cases:—namely, craw-craw, elephantiasis and lichenification.

A NEW SPECIES OF FILARIAL LARVA FOUND IN THE SKIN OF NATIVES IN THE GOLD COAST. J. W. F. Macfie and J. F. Corson, Ann. Trop. M. & Parasitol. **16**:465 (Dec. 30) 1922.

This parasite was found in the skin of many natives being examined for other larvae, especially in those presenting lichenification and dermal thickening. Its pathogenicity had not been determined, but the authors propose the name of *Agamofilaria streptocerca*.

Jamieson, Detroit.

TREATMENT OF CHRONIC ECZEMA WITH CONCENTRATED CARBON ARC LIGHT (FINSEN). Svend Lomholt, Brit. J. Dermat. & Syph. **35**:45, 1923.

Lomholt reports the result of the treatment of chronic eczema in various stages with the Finsen light: In 100 patients thus treated, about 60 per cent. were completely cured, about 25 per cent. were more or less improved, and in only 15 per cent. were the results only transitory or negative. The cases most suitable for treatment are the old dry infiltrated and keratotic ones, but many vesicular cases were favorably influenced. The exposures given are much shorter than those used when the light is used for the treatment of lupus vulgaris. The method is laborious and expensive, and must be limited to cases uninfluenced by ordinary methods of treatment. The author states that the use of the carbon light possesses certain advantages over roentgen-ray treatment, as it can be used repeatedly without damage to the skin, and it never aggravates the disease.

A WASSERMANN MICRO-TECHNIQUE NEEDING ONLY OCCASIONAL TITRATION OF THE COMPLEMENT. Robert Donald, Brit. J. Dermat. & Syph. **35**:50, 1923.

In this article is described in detail a method requiring only infrequent titration of complement, the latter being obtained from an ear vessel of one or more duly titrated guinea-pigs, the latter doing service for several years each. This permits standardization of the Wassermann test by the use of identical complement "on tap."

Senear, Chicago.

ORIENTAL SORE (CUTANEOUS LEISHMANIASIS) IN THE UNITED STATES. R. A. Lambert, J. A. M. A. **80**:986 (April 7) 1923.

This is a report of two cases of the disease occurring in immigrant Armenian children. In one of the cases, the incubation period was at least six months. It is suggested that biopsy be made for diagnostic purposes, as the organism is more easily found in stained tissue than in smears. Treatment of one of the patients by excision and roentgen-ray was successful. The other case involuted spontaneously after a year. Ten cases of this disease have been reported in the United States in the last two years.

KERATODERMIA BLENNORRHAGICA. H. L. KRETSCHMER, J. A. M. A. **80**:993 (April 7) 1923.

The author herewith reports a case of triad urethritis, arthritis and hyperkeratotic lesions. A urethral discharge was present for more than two years when the skin lesions first appeared. The latter were typical, as shown by four excellent illustrations. The aim of treatment is the removal of the infective process usually found in the prostate gland or seminal vesicles. Vaccines have given varying results. The case reported herein was not followed to completion.

NEW TECHNIC FOR THE FLOCCULATION TEST OF SYPHILIS. A. R. CASILLI, J. A. M. A. **80**:1068 (April 14) 1923.

This is a short preliminary report of a new modification of the flocculation test. It is said to give sharp, clear reactions which are in perfect accord with the Wassermann test.

THE WASSERMANN REACTION IN SCARLET FEVER PATIENTS. G. E. CHRISTENSEN, J. A. M. A. **80**:1118 (April 21) 1923.

In 110 cases of scarlet fever, the Wassermann reaction was positive ten times, but only with cholestorolized antigens. The positive reactions were only transitory. Positive Wassermann reactions occur as a result of scarlet fever, but are usually weak. A strongly positive reaction in scarlet fever is as good evidence of syphilis as at any other time.

PROTEIN SENSITIVITY IN CHILDREN WITH NEGATIVE CUTANEOUS REACTIONS. E. S. O'KEEFE, J. A. M. A. **80**:1120 (April 21) 1923.

In infantile eczema a certain percentage of cases giving negative cutaneous reactions can be demonstrated clinically to be due to protein sensitization. The negative reactions are not due to temporary desensitization, because they are presistently absent. O'Keefe advances the hypothesis that there is a variation of the threshold of sensitivity in the various tissues, and that this accounts for the lack of response of the skin in these cases. The threshold of the sensitivity may likewise be the factor which determines whether hayfever, asthma or eczema will result from foreign proteins with which the tissues are brought in contact.

POSITIVE WASSERMANN REACTION IN A FATAL CASE OF ESTIVO-AUTUMNAL MALARIA. G. M. MCCONNELL, J. A. M. A. **80**:1123 (April 21) 1923.

The patient had a four plus Wassermann reaction during the febrile stage of the disease. No clinical significance was accorded the reaction, as it was thought to be due to malaria. At necropsy, however, syphilitic lesions of the aorta were found.

AUTOSERUM TREATMENT OF PNEUMOCOCCUS MENINGITIS COMPLICATED BY SYPHILIS. W. S. HORN, J. A. M. A. **80**:1124 (April 21) 1923.

Intraspinal injection by autoserum has been used with considerable success in nonspecific meningitis, but it has been considered contraindicated in cases

of the disease complicated with syphilis, because of the theoretic possibility of spreading the latter disease to the meninges. To refute this conception, as well as to add something to the therapy of the condition, Horn reports an applicable case in which a modified Swift-Ellis treatment was administered and apparently was the cause of the favorable outcome.

CHRONIC PURPURIC ERUPTION WITHOUT DEMONSTRABLE BLOOD CHANGES. J. H. ARNETT and F. D. WEIDMAN, J. A. M. A. **80**:1132 (April 21) 1923.

In this case, there were long-standing cutaneous hemorrhages, a positive tourniquet test for capillary permeability and a normal platelet count. Histologic examination revealed acute telangiitis. This accounted for the clinical picture. The case presented some of the features of Majocchi's disease, but it diverged from it too much to be so diagnosed. The cause was not determined. The authors consider the case primary telangiitis with purpura.

DIETARY CONSIDERATION IN INFANTILE ECZEMA. J. R. GERSTLEY, J. A. M. A. **80**:1141 (April 21) 1923.

The author believes that diet plays only a secondary part in infantile eczema. Diet affects eczema in only two ways: (*a*) by affecting the nutrition of the whole child, and (*b*) by affecting the amount of fluid in the tissues. The diet which has greatest influence on the disease is that which brings the child to the best possible state of nutrition. Dietary restriction is indicated only in overfed babies, and in those with secondarily infected eczema. In the latter cases, a temporary reduction of diet by depleting the tissues of fluids leaves the tissue less fertile for bacterial growth.

MICHAEL, Houston, Texas.

STUDIES ON THE CHANGES PRODUCED BY ROENTGEN RAYS IN INFLAMED CONNECTIVE TISSUE. A. A. MAXIMOW, J. Exper. M. **37**:319 (March) 1923.

The cells chiefly affected by the action of roentgen rays on inflamed tissue were found to be the fibroblasts which received a strong inhibitory influence following the dose used in the experiments. The reaction apparently depends on both the roentgen ray and the presence of inflammation and does not follow either one alone. This should always be kept in mind in the treatment of malignant tumors in which there is some inflammatory irritation. The article also goes minutely into other pathologic changes induced by the roentgen ray in tissue experimentally inflamed.

THE INCREASED ABSORPTION OF X-RAYS BY VITALLY STAINED WHITE RATS. W. M. BALDWIN, J. Exper. M. **37**:357 (March) 1923.

Using a dose of roentgen rays which produced death in unstained rats in from 110 to 120 hours, the hours of viability were shortened to from sixty to seventy by injection of vital stains, such as trypan blue. The cause of death in these rats had not been determined, and there was also considerable variation in susceptibility in the stained rats.

EXPERIMENTAL OBSERVATIONS ON THE PROPHYLAXIS AND TREATMENT OF SYPHILIS. H. J. NICHOLS and J. E. WALKER, J. Exper. M. **37**:525 (April) 1923.

Two methods of inoculation were employed to test the efficacy of 30 per cent. calomel ointment. Scarification and inoculation of the scrotum was 100 per cent. successful, gland transfers giving 87.5 per cent. of takes. Up to eight hours after inoculation the calomel ointment prevented infection, regardless of whether the ointment base was hydrous wool fat and petrolatum or benzoated lard and wax. In some rabbits, the absorption of mercury was sufficient to produce death after applying a large amount of the ointment.

Rabbits inoculated by gland transfer were treated with the original arsphenamin and neo-arsphenamin, and none showed evidence of syphilis even after one injection. The authors believe from these experiments that arsphenamin has successfully eradicated syphilis in rabbits, and that sufficient treatment can accomplish the same result in man, although rabbits and man may not respond alike to the action of the drug.

Natural spirochetosis of rabbits need not be a serious complicating factor in experimental syphilis, except when lesions of generalized syphilis involve the genitalia, and in sexual transmission experiments.

PLANT DERMATITIS. H. N. RIDLEY, J. Trop. M. **25**:225 (July 15) 1922.

Attention is called to an erysipeloid condition appearing in persons coming in contact with tropical and subtropical plants and trees of the order *anacardiaceae*. The action of the sap on the skin is described as similar to that of the poisonous principle from which the Japanese lac is made. Thorough application of oil is said to be a preventive, and the use of an alkaline powder will counteract the action of the poison.

ANTIMONY AND SULPHUR IN THE TREATMENT OF LEPERS. F. G. CAWSTON, J. Trop. M. **25**:345 (Nov. 1) 1922.

This is a note to support a previous contention that sulphur should be combined with antimony in the treatment of lepers. The writer had previously treated lepers with some success by using Oppenheimer's colloidal antimony combined with sulphur.

JAMIESON, Detroit.

ACUTE ANAPHYLACTIC REACTION FOLLOWING THE INTRAVENOUS INJECTION OF ARSPHENAMIN. P. B. THOM, New York State J. M., April 1, 1923.

The author reviews briefly the various theories which have been advanced to account for the acute reaction occasionally observed following secondary injections of arsphenamin. While acknowledging that a few of them may be due to impurities in the drug or in the water used, he concludes that the vast majority depend on sudden flocculation in the blood or lysis of the formed elements, both of which are due to physical qualities of the injected material in a susceptible person. The commonest errors are the use of a solution which is too concentrated, which is hypotonic, or which contains an excess of alkali. The reaction may be prevented by the preliminary injection of one-fifth of the therapeutic dose twenty-four hours before the therapeutic

dose is to be given, or by the injection of 60 c.c. of a 2 per cent. solution of sodium bicarbonate five minutes before the injection of the arsenical solution.

The author prefers neo-arsphenamin because it is practically free from the dangers which attend the use of arsphenamin, because it is easier to prepare, and because the therapeutic results are equally good if a sufficient dosage is given.

WILLIAMS, New York.

THE TUBERCULIDS SHOULD BE CALLED "TUBERCULOIDS." J. DARIER, Bull. Soc. franç. de dermat. et. syph. **30**:112, 1923.

In 1896, Darier proposed the name "tuberculids" for this group of dermatoses, but various authors have lately shown that these same manifestations can be caused by nontuberculous infections, especially syphilis, which would make the designation "tuberculoid" preferable. Then such a lesion, if due to syphilitic infection, would be called a "syphilitic tuberculoid."

ALOPECIA AREATA WITH SYMPATHETIC NERVOUS DERANGEMENTS IN A PATIENT WOUNDED DURING THE WAR. THE ENDOCRINE-SYMPATHETIC ORIGIN OF ALOPECIA AREATA. LEVY-FRANCKEL and JUSTER, Bull. Soc. franç. de dermat. et syph. **30**:113, 1923.

The authors have seen alopecia areata follow wounds in four cases. They describe the case of a man aged 32 years, whose right arm had been injured by a shell in 1918, local nerve lesions having resulted. Since 1921, bald patches on the scalp had appeared at varying intervals, and examination revealed a diminution of the pilomotor reflex, disturbances of sweat production and of the vasomotor tone, accompanied by signs of hyperthyroidism and of gonadal deficiency.

A LESION OF THE BRACHIAL PLEXUS DUE TO SHOULDER DISLOCATION; CUBITAL AND MEDIAN CAUSALGIA; PALMAR KERATODERMA. LEVY-FRANCKEL, JUSTER and RIMET, Bull. Soc. franç. de dermat. et syph. **30**:116, 1923.

Two such cases are reported, in the first of which potassium iodid ionization of the affected nerve trunks was followed by the disappearance of the keratoderma. There were signs of endocrine and sympathetic nervous disturbances.

A CASE OF PAPULONECROTIC AND NODULAR TUBERCULIDS OF THE FACE. LOUSTE, THIBAUT and G. BARBIER, Bull. Soc. franç. de dermat. et syph. **30**:120, 1923.

In a robust man, aged 30 years, these lesions had involved the face and neck for seven months. In view of the fact that the tuberculin reaction was very slow and mild, and that the response of the lesions to subcutaneous injections of Jousset's tuberculous vaccine was nil, the etiology was open to doubt.

ACQUIRED SYPHILIS IN AN INFANT; A CASE OF CONTAMINATION DURING BIRTH. DUMET (HUDELO), Bull. Soc. franç. de dermat. et syph. **30**:123, 1923.

The mother had been infected during the eighth month of pregnancy, vulvar lesions appearing, and the child soon presented five primary sores on the scalp.

ZONIFORM LEUKODERMA OF THE RIGHT FLANK; A BAND OF SCLERODERMA WITH ATROPHY EN MASSE OF THE LEFT LOWER EXTREMITY; VERTEBRAL ANOMALIES: SACRALIZATION, SPINA BIFIDA OCCULTA. A. Leri and L. Lamy, Bull. Soc. Franç. de dermat. et syph. **30**:127, 1923.

In a child aged 8 years, the cutaneous manifestations were said to have been present for four years, and the authors consider it likely that these and the vertebral anomalies are the results of arrested development of the central nervous system.

SYPHILITIC LEUKODERMA, REAPPEARING SYMETRICALLY AND IRREGULARLY FOLLOWING THE NERVE DISTRIBUTION; A HIDDEN VERTEBRAL LESION AT THE CORRESPONDING LEVEL. A. Leri, Bull. Soc. franç. de dermat. et syph. **30**:120, 1923.

In a man, aged 64 years, with syphilis of thirty years' duration, the leukoderma, present for ten years, may have been caused by a demonstrable vertebral lesion.

CHRONIC ECZEMA OF THE BREASTS AND AMENORRHEA IN A YOUNG GIRL. L. Lortat-Jacob and P. Legrain, Bull. Soc. franç. de dermat. et syph. **30**:134, 1923.

The eruption had been present for eighteen months, the patient being 21 years of age and presenting symptoms of hypothyroidism.

A NOTE ON THE VARIATIONS OF THE VAGOSYMPATHETIC EQUILIBRIUM IN THE COURSE OF SOME ERYTHEMAS. M. Laurent, Bull. Soc. franç. de dermat. et syph. **30**:134, 1923.

In seventeen cases of syphilitic roseola and several of erythema medicamentosum and erythema multiforme, the oculocardiac reflex was tested, and a coexisting sympatheticotonia was found, both apparently being manifestations of a defensive reaction.

A SEARCH FOR SYPHILIS, ACQUIRED OR CONGENITAL, IN A SERIES OF TWENTY-EIGHT PSORIATIC PATIENTS. Leredde, Bull. Soc. franç. de dermat. et syph. **30**:138, 1923.

The author found suggestions of syphilitic infection in twenty-one of the patients; in six, neo-arsphenamin was given, followed by the disappearance of the lesions in five and an exacerbation in the sixth.

PREGNANCY IN A SYPHILITIC PATIENT; SUBCUTANEOUS ARSENICAL TREATMENT; THE CHILD STILLBORN AND MACERATED. Halbron and Barthelemy, Bull. Soc. franç. de dermat. et syph. **30**:147, 1923.

Infected in 1921, the patient had received several courses of neo-arsphenamin by the subcutaneous route, and late in pregnancy four intravenous injections of sulpharsphenamin, but to no avail.

TABETIC OSTEO-ARTHROPATHIES OF BOTH HIPS. R. Barthelemy, Bull. Soc. franç. de dermat. et syph. **30**:147, 1923.

In this case there was rarefaction of the bone at certain points, and proliferation at others.

LOCALIZED ERUPTIONS FOLLOWING INJECTIONS OF ARSPHENAMIN. LACAPERE and LEPINAY, Bull. Soc. franç. de dermat. et syph. **30**:149, 1923.

In two patients with secondary syphilis, the authors noted the appearance of an evanescent urticarial lesion, the forehead being involved in one case and the eyelid in the other. There were no signs of arsenical intoxication, and since the intensity of the outbreaks diminished with succeeding injections of the arsenical drug, the authors concluded that they were dealing with sensitization.

URTICARIA DUE TO BISMUTH INJECTIONS. E. LEPINAY, Bull. Soc. franç. de dermat. et syph. **30**:150, 1923.

A man, aged 25 years, had been treated with neo-arsphenamin and mercurial (gray) oil uneventfully for thirteen months, but two months after the interruption of this treatment the intramuscular injection of 2 cc.c. (0.2 gm.) of quinin iodobismuthate was followed by a severe urticarial outbreak. The subsequent injection even of small doses was followed by a similar intense reaction.

PROGRESSIVE MUTILATING SCLERODERMA. ROUDINESCO and P. VALLERY-RADOT (MARFAN), Bull. Soc. franç. de dermat. et syph. **30**:151, 1923.

In a boy, aged 13 years, the distal two thirds of both forearms, several toes, and parts of the nose and ears had been destroyed. On each side of the scalp there was a bald patch suggesting roentgen-ray alopecia, but it was stated that no roentgen rays had been applied.

CONGENITAL LYMPHANGIOMA; ANGIOMA PLANUM; KERATOTIC NEVUS. LOUSTE and DAUPTAIN, Bull. Soc. franç. de dermat. et syph. **30**:155, 1923.

The hypogastric and right inguinal regions and the right thigh and buttock were involved in a girl aged 16 years, and the authors found that the nevi followed the nerve distribution in an interesting manner.

VACCINIA GENERALIZED BY MULTIPLE INOCULATIONS IN A PATIENT WITH ECZEMATOID PRURIGO. L. LORTAT-JACOB, LEGRAIN and SOLENTE, Bull. Soc. franç. de dermat, et syph. **30**:156, 1923.

The left arm, shoulder and upper thorax were the sites chiefly involved.

HYPERKERATOSIS OF THE THENAR EMINENCE LIMITED TO THE REGION SUPPLIED BY THE SEVENTH CERVICAL NERVE SEGMENT, RELATED TO A RADICULAR OBSTETRICAL PARALYSIS ACCOMPANIED BY SYMPATHETIC DISORDERS. L. LORTAT-JACOB, LEGRAIN and P. LEFEVRE, Bull. Soc. franç. de dermat. et syph. **30**:157, 1923.

The authors stress the apparent relationship between the root injuries and the sympathetic nervous disturbances. The muscles supplied by the fifth, sixth and seventh cervical segments were involved.

BILATERAL HYDRARTHROSIS OF THE KNEES AS A SIGN OF CONGENITAL SYPHILIS. J. Roederer and A. Lix, Bull. Soc. franç. de dermat. et syph. **30**:R.S.2, 1923.

In a boy, aged 16 years, who had apparently been well until one year previously, there were bilateral knee involvement, double interstitial keratitis and a positive Wassermann reaction. Improvement followed the employment of combined arsenical and mercurial treatment. The Wassermann reaction of fluid aspirated from the affected joints was positive.

ORIENTAL SORE (ALEPPO BUTTON). Pautrier and O. Eliascheff, Bull. Soc. franç. de dermat. et syph. **30**:R.S.4, 1923.

With the aid of a picture, the authors describe the case of a boy, aged 16 years, with a typical lesion on the dorsum of the left hand. Tissue sections were found to contain the causative organisms, and the ulcer healed readily under the application of moist compresses. The infection occurred in Algiers.

VEGETATING FOLLICULAR PSOROSPERMOSIS (DARIER'S DISEASE). Escher (Pautrier), Bull. Soc. franç. de dermat .et syph. **30**: R.S.5, 1923.

An eruption of three years' duration, in a man aged 21 years, had a predilection for the face, axillae, abdomen and midback, the elementary lesion being a small follicular epidermal papule, surmounted by a scale. There were no vegetations. The affected skin was curiously freckled. A biopsy specimen could not be obtained, but corps ronds were found in scarpings.

GIANT LICHENIFICATION OF THE GENITAL FOLDS. Pautrier and J. Roederer, Bull. Soc. franç. de dermat. et syph. **30**:R.S.7, 1923.

This condition, which had been present for five months in a woman, aged 70 years, presented such tumefaction that diagnoses of fibroma and malignant tumors had to be excluded. The histologic findings are reported, and there are two illustrations of the gross lesions.

SCLERODERMA TREATED BY POLYGLANDULAR ENDOCRIN THERAPY. Hugel, Bull. Soc. franç. de dermat. et syph. **30**:R.S.10, 1923.

This patient had been presented one year previously, and the condition had since been entirely cured by polyglandular treatment, which in the author's opinion deserves a trial in every case of scleroderma.

RESULTS OF ARSPHENAMIN TREATMENT OF SYPHILIS DURING PREGNANCY. E. Bodin, Bull. Soc. franç. de dermat. et syph. **30**:R.S.11, 1923.

The author advocates the use of arsenical treatment alone, believing it superior to the mixed treatment. Among twenty patients presenting active syphilitic lesions early in pregnancy, eighteen children were born, and there were only two miscarriages. In a series of eight instances of latent syphilis treated by this means, there were eight healthy infants born at term. These children have been observed for from two to seven years, but no signs of the disease have appeared.

POST-TRAUMATIC CUTANEOUS EPITHELIOMAS. HICKEL and OBERLING (PAUTRIER), Bull. Soc. franç. de dermat. et syph. **30**:R.S.15, 1923.

In two cases, the authors present histologic proof that prickle cell epitheliomas arose soon after injury. The first case was that of a man, aged 45 years, who developed an epithelioma on the hand at the site of injury by a splinter six weeks previously. In the second case, that of a man aged 22 years, the epithelioma appeared at the site of a burn on the lower lip, which had been sustained two years previously.

TWO CASES OF DERMATOMYOMA. A. DISS (PAUTRIER), Bull. Soc franç. de dermat. et syph. **30**:S.R.20, 1923.

A pea-sized tender tumor was removed from the thigh of a man aged 56 years; it had been present for one month, according to the patient. Histologic study showed that it had apparently arisen from the musculae arrectores pilorum. A small nut-sized tumor was excised from the forearm of a man aged 22 years; it had been present for a few months, and had never been painful. After histologic examination, the author concluded that it was probably a muscular nevus with malignant tendencies.

SOLUBLE SALT OF BISMUTH IN CUTANEOUS SECONDARY AND TERTIARY SYPHILIS. GOUIN and JEGAT, Bull. Soc. franç. de dermat. et syph. **30**:R.S.39, 1923.

If given intramuscularly, the administration must be slow, in order to avoid pain. In the authors' experience, this drug seemed fully as active as neo-arsphenamin, if not more so, a Herxheimer reaction having followed its immediate energetic employment in active secondary cases. The effect on condylomas and mucous patches is said to be especially striking.

PROGRESSIVE SCLERODERMA WITH SCLERODACTYLY AND GENERALIZED MELANODERMA. SPILLMANN and DROUET, Bull. Soc. franç. de dermat. et syph. **30**:R.N.6, 1923.

In a farmer, aged 32 years, this condition was of scarcely a year's duration, having begun with pains in several joints. There was some degree of asthenia. Thyroid and suprarenal therapy had been tried without benefit, and the result of pituitary administration had been negative. Slight improvement had followed the internal and external use of potassium iodid.

ATYPICAL SCLERODERMA; HYPERTHYROIDISM. ETIENNE, Bull. Soc. franç. de dermat. et syph. **30**:R.N.7, 1923.

There were bilateral ulnar bands, adherent to the subjacent muscles, and histologic study showed them to be purely fibrous.

SCLERODERMA IN PLAQUES, TREATED AND CURED BY IONIZATION WITH POTASSIUM IODID. J. WATRIN, Bull. Soc. franç. de dermat. et syph. **30**:R.N.8, 1923.

Immersing the negative electrode in a 5 per cent. solution of potassium iodid, the author at first gave exposures lasting twenty-five minutes with from 25 to 30 milliamperes, at intervals of fifteen to twenty days, later gradually increasing the time to forty-five minutes and the milliamperes to 35 or 40.

VERMICULATE ATROPHODERMA OF THE CHIN WITHOUT FOLLICULAR KERATOSES. SPILLMANN, Bull. Soc. franç. de dermat. et syph. **30**:R.N.10, 1923.

In a girl aged 19 years, this condition had been present since puberty. Darier considered the case a good example of that rare entity.

TREATMENT OF LARGE KELOIDS BY SOLID CARBON DIOXID. SPILLMANN and MOUTON-CHAPAT, Bull. Soc. franç. de dermat. et syph. **30**:R.N.11, 1923.

In treating keloids following burns on a girl's lower extremities, pepsin applications and radiotherapy had been employed without favorable results, but the application of solid carbon dioxid by means of the cryocautery was most effective.

SYPHILIS AND TATTOOING. SPILLMANN, DROUET and DIOT, Bull. Soc. franç. de dermat. et syph. **30**:R.N.12, 1923.

In a patient with a severe papulosquamous syphilid, the red tattoo marks were occupied by many lesions, while the blue marks were not involved.

EPITHELIOMATOSIS EN NAPPE OF THE THORAX AFTER THE ABLATION OF A CANCER OF THE BREAST. SPILLMANN, Bull. Soc. franç. de dermat. et syph. **30**:R.N.13, 1923.

In a woman, aged 48 years, this condition followed eighteen months after breast amputation. It was verified histologically.

LYMPHANGIECTASES ARISING ON A SURGICAL CICATRIX. SPILLMANN and WATRIN, Bull. Soc. franç. de dermat. et syph. **30**:R.N.14, 1923.

According to the patient, a man, aged 20 years, a lipoma had been removed from the shoulder ten years previously. Lymphangiectases had subsequently appeared. The original tumor may have been a lymphangioma.

NEVOCARCINOMA OF THE LOWER EYELID CURED BY TWO ELECTROLYTIC TREATMENTS. WATRIN, Bull. Soc. franç. de dermat. et syph. **30**:R.N.14, 1923.

The lesion, in a woman aged 62 years, had been present more than five years, and had been cauterized previously, which had only served to stimulate its rate of growth. Electrolysis, with 6 to 7 milliamperes, was used with apparently excellent results, three months having elapsed uneventfully since that time.

THE THREE PLANES OF DIAGNOSIS IN DERMATOLOGY. J. DARIER, Bull. Soc. franç. de dermat. et syph. **30**:R.N.15, 1923.

According to the author, these are the morphologic, etiologic and pathogenic findings, which of course also have an important bearing on the treatment.

PARKHURST, Toledo, Ohio.

DISTURBANCE CAUSED BY NEO-ARSPHENAMIN AND HOW TO PREVENT THEM, WITH SPECIAL REFERENCE TO EPINEPHRIN. REINHARD-EICHELBAUM, Deutsch. med. Wchnschr. **48**:804, 1922.

From five to ten minutes previous to an arsphenamin injection the author injects from 0.5 to 0.75 c.c. of a 1:1,000 solution of epinephrin. This prevents the vasomotor syndrome frequently caused by arsphenamin. It also allows an increase in the single arsphenamin dose. In all cases the author advises this as a routine prophylactic measure.

THE "ACTIVATION" OF THE BODY CELLS. STUDIES ON IMMUNITY AND VIRULENCE. WEICHARDT, Klin. Wchnschr. **35**:1725, 1922.

The effect of therapy with protein substances has been explained as an "activation" of plasma and cells. This "activation" is not identical with stimulation. Bacteria can be activated just as can body cells, that is to say, their growth and toxin producing ability can be increased.

ANTIBODIES IN TUBERCULOSIS. COMPLEMENT BINDING REACTION IN TUBERCULOSIS AND ITS RELATION TO MALARIA. HEINEMANN, München. med. Wchnschr. **69**:1035, 1922.

The author studied syphilis and tuberculosis in the natives of Java. Tabes and progressive paralysis were not seen. The author believes that malaria causes a defensive reaction of the system which affects the subsequent syphilis. Few natives escape infection with malaria. This is believed by the author to stimulate the defensive action of the body in the nonspecific sense.

ROENTGEN-RAY NAUSEA. SIMONS, Strahlentherapie. **14**:106, 1922.

The author believes that roentgen-ray nausea is due to direct influence on the nerves of the intestinal tract. He therefore advises medication with valerian tablets (Bornyvaltablets-Riedel).

IRRADIATION TECHNIC IN THE REGION OF THE MALE PELVIS. LENK, Strahlentherapie **14**:112, 1922.

Lenk noticed that irradiation of the lower abdominal region of the male caused azoospermia even though the scrotum had been carefully protected with a 0.5 mm. lead rubber bag. This is due to the scattering of the alpha rays. The author says the testicles should be drawn well down into the scrotum and held in position with a peg, the entire scrotum being covered with a lead rubber bag.

CARCINOMA, WITH SPECIAL REFERENCE TO IMMUNITY. CASPARI, Ztschr. f. Krebsforschung, **19**:74, 1922.

The author believes in both specific and nonspecific immunity because the serum of rabbits which had been vaccinated with mouse sarcoma was more toxic for normal mice than the serum of normal rabbits, but not for mice which suffered from sarcoma.

AHLSWEDE, Buffalo, N. Y.

Society Transactions

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, April 24, 1923

W. B. Trimble, M.D., *President*

A CASE FOR DIAGNOSIS (PHENOLPHTHALEIN ERUPTION). Presented by Dr. Howard Fox.

Miss K., aged 40, first noticed the eruption five months ago. It had recurred at intervals of from seven to ten days in discrete patches on the trunk and on the backs of the hands. The lesions appeared at each outbreak in the same areas and were very itchy. There had been one month of remission during the past five months following dietary restriction. She had been treated by other physicians with colon irrigations without appreciable benefit. She denied having taken any proprietary medicines, except an occasional aspirin tablet and some bromid during the past two weeks. Examination revealed an eruption on the upper part of the back, on the chest and on the backs of the hands, consisting of about twenty-four round or oval, purplish, smooth spots, varying in size from that of a pea to that of a quarter of a dollar. On the abdomen and thigh were two pigmented brownish macules where formerly reddish lesions had existed. These were suggestive of the persistent pigmentation seen in phenolphthalein rashes. The patient was an intelligent woman of slender build.

DISCUSSION

Dr. Schwartz said he had seen the patient in private practice and could obtain no history of the use of any drug. He was inclined to consider the eruption some form of toxic erythema. It had cleared up several times by restriction of the diet, colon irrigations, etc., only to recur at irregular intervals without any apparent cause.

Dr. Wise said that the patient had been under his care for six weeks, and the history was strongly negative in regard to any drug eruption. He had been very much puzzled about a diagnosis and he was still puzzled. The microscopic report was not decisive, and the closest diagnosis they could make was lupus erythematosus; it seemed possible that it might be a disseminated form of lupus erythematosus, which comes and goes in "crops." He felt almost sure that it was not a drug eruption. The microscopic section did not resemble that of phenolphthalein eruption.

Dr. Bechet said he would not have thought of lupus erythematosus. With the absence in the history of drug ingestion, he would call it an ordinary erythema perstans, or better still, a recurrent, persisting erythema multiforme.

Dr. Lane asked whether erythema perstans was followed by pigmentation as deep as that presented by this patient.

Dr. Wise said he did not understand how one could call any condition that did not persist "perstans." These lesions disappeared and came back again, so it could not be erythema perstans strictly speaking.

DR. HIGHMAN said the adjective "perstans" was simply a relative term. The lesions do disappear but tend to recur at the same site. According to Tileston's and Crohn's description of rat bite fever, this phenomenon was characteristic of that disease. As to the pigmentation, that too was seen in erythema perstans as deep at times as slate. In his opinion, it was clinically a case of erythema perstans, the etiology being unknown. The lesions were a little unusual, some of them being less rigid as to outline. As to the question of lupus erythematosus disseminatus, it seemed probable that when this group was studied more carefully, many cases would be found to be unrelated to lupus erythematosus, but would prove variants of multiform erythema, notably erythema perstans.

DR. TRIMBLE said that if the eruption were erythema perstans, one would expect it to persist; but he agreed with Dr. Highman that the recurrences were persistent, the lesions not being so persistent, but recurring.

DR. HOWARD FOX said that the patient certainly had a persistent recurring erythema in certain circumscribed patches, and one of the patches had the marked pigmentation seen in phenolphthalein eruptions. As Dr. Wise said, an intelligent history merited some attention, and it was true that the patient gave no history of having taken phenolphthalein. Dr. Fox said he was unable to make a diagnosis in this case.

A CASE FOR DIAGNOSIS. (SARCOID?) Presented by DR. HOWARD FOX.

Mrs. C. L., aged 65, a widow, born in the United States, was first seen in May, 1921. At that time she presented a group of five nodules on the forehead above the left eye. The largest of these lesions had been present for twenty years. The four smaller ones had been present for four months. They were bluish red, smooth and firm, with a cystic feeling. The Wassermann test was negative. A tentative diagnosis of sarcoid was made at that time. The patient was given one exposure of unfiltered roentgen ray (three-fourths skin unit), and at the end of three weeks the tumors had entirely flattened, leaving reddish spots which had persisted. There had never been a return of these original tumors. In August, 1922, another tumor appeared on the left malar prominence; it was excised by her family physician, but soon reappeared. She now presented two separate hemispherical, firm, dull red tumors, the largest being three quarters inch (19.05 mm.) long, and one quarter inch (6.35 mm.) in height. A biopsy had recently been made by the actual cautery. A few hours before presentation she had fallen and bruised one of the tumors. The patient was a woman of small size in apparent good health.

DISCUSSION

DR. FORDYCE said he considered the condition one of sarcoma rather than one of sarcoid.

DR. WISE and DR. HIGHMAN said they believed the condition was sarcoma.

DR. HOWARD FOX said he had not been able to decide between sarcoid and sarcoma, the two most probable diagnoses. One of the lesions, which he had treated two years ago, had existed for twenty years, had disappeared after one roentgen-ray treatment and had remained well until the present time. The new lesions which the patient now presented were similar in appearance, and it therefore seemed probable that they were sarcoid and not sarcoma.

LICHEN PLANUS WITH LESIONS ON ELBOWS RESEMBLING PSORIASIS. Presented by Dr. Howard Fox.

H. L., aged 28, an advertising man, born in the United States, first noticed an eruption about a month ago. It spread rapidly and became generalized on the trunk and extremities. The lesions were partly discrete and partly confluent. There were typical lichen planus papules, especially well merked on the forearms and glans penis. On the thighs were small circinate crateriform lesions. The eruption, which was somewhat sparse, showed in general a noticeable absence of scaling, characteristic of psoriasis. No ointments of any kind had been previously used. The mucous membrane of the mouth was apparently normal. The patient was presented on account of small scaly patches on the elbows which were moderately infiltrated and covered with whitish silvery scales, giving a typical picture of psoriasis.

DISCUSSION

Dr. Fordyce said that Dr. Fox had called atention to the lesions, parts of which presented the appearance of lichen planus, while other parts looked like typical psoriasis. It was an interesting combination of what might be two separate conditions.

Dr. Bechet said that if the two dermatoses could co-exist in the same patient —and he did not see why such a thing was impossible—the case presented two distinct dermatologic conditions. The lesions were typical of both diseases.

Dr. Lane said he thought that Dr. Fox's diagnosis of lichen planus was probably correct.

Dr. Wise also agreed with the diagnosis of lichen planus.

Dr. Howard Fox said that the patient had been carefully examined by daylight both by him and by his assistants, and that an unquestioned diagnosis of lichen planus had been made. There were many typical lichen planus papules, some being situated on the glans penis. There were also circinate crateriform lesions on the thigh, and there was a general and notable absence of scaling. The patches on the elbows looked like a typical psoriasis, and such a diagnosis would have been made if no other lesions had been present. It did not seem probable that both psoriasis and lichen planus should appear for the first time almost simultaneously.

LUPUS VULGARIS RESEMBLING LUPUS ERYTHEMATOSUS. Presented by Dr. Wise for Dr. Fordyce.

Mrs. M. G., aged 40, born in Italy, a housekeeper, had had the present condition for eight years. On the nose and right side of the cheek there were erythematous, marginated, scaly patches with indurated borders, one of them extending to and involving the mucosa of the upper lip. Diascopy revealed distinct apple-jelly nodules. On the left cheek were three similar discrete dime-sized lesions. The disease started on the nose (where now the skin was atrophic) and spread to the other areas.

DISCUSSION

Dr. Lane and Dr. Fox agreed with the diagnosis of lupus vulgaris.

Dr. Fordyce said he considered the case one of lupus vulgaris with a superficial resemblance to lupus erythematosus. He had always doubted the combina-

tions of the two conditions, but in a case recently studied by Dr. Cannon at the Vanderbilt clinic, giant cells had been found in a case which was clinically lupus erythematosus. A brief reference only was made at this time to the case in question, as Dr. Cannon was following up his histologic studies and would report later on his findings.

Dr. Highman said he believed the case represented the type of erythematous lupus vulgaris described by Leloir as lupus vulgaris erythematodes, which was redescribed fourteen years ago by Kyrle in a patient examined in Vienna, in which clinical discoid lupus erythematosus proved histologically to have lesions of lupus erythematosus on one side and lupus vulgaris on the other. The condition has been recognized in France and in German speaking countries for fifteen or twenty years.

Dr. Wise agreed with the diagnosis of lupus vulgaris, but what made that diagnosis seem doubtful was the fact that the patient was 50 years old and had had these lesions only six years, which was rather late in life to acquire lupus vulgaris. A biopsy would be made and reported later.

Dr. Trimble referred to the age of the patient and told of cases of adults in which he had seen tuberculous infection on the mucous membrane of the nose, on the borders and on the face. A so-called type of lupus vulgaris of the skin would transform itself into papules outside and prove to be lupus vulgaris, which would prove that a patient of 30 or 40 who had this infection might later have lupus vulgaris on the face.

Dr. Bechet, in reference to Dr. Wise's remarks relative to the infrequency with which lupus vulgaris was noted as beginning late in life, stated that he had presented before the Academy Section several years previously a case of lupus vulgaris in a man of 65. It was located on the cheek, and had been present for only three years. A biopsy confirmed the clinical diagnosis.

DERMATITIS LICHENOIDES CHRONICA ATROPHICANS. Presented by Dr. Wise for Dr. Fordyce.

Mrs. S. G., aged 29, a married woman, born in Russia, who had been in this country for eleven years, who did ordinary housework, said she had had an eruption for three months, but that seemed doubtful. She presented lesions on the chest, back and wrists, but none in the mouth. The eruption consisted of plaques that were dollar-sized and larger, made up of millet seed to split-pea sized, depigmented, slightly depressed, thin, dry, atrophic spots, with some hyperpigmentation around each atrophic area. There were no definite lichen papules present, nor was any cardboard infiltration noticed at the present time. The patient had had one miscarriage, three children living and well, and one child that died of tuberculosis. She seemed to be in good health, and her Wassermann test was negative. A section taken for microscopic study had not been reported on as yet.

DISCUSSION

Dr. Williams remarked that it was one of those atrophying scleroses, and it seemed a pity that the word lichen or lichenoid should be used in describing it, for there was little or nothing in it to suggest lichen.

Dr. Highman said he did not think if there was such a thing as the lichen albus of von Zumbusch that this was a case of it, judging from the examples that he had seen in Europe. He had a distinct impression that in addition to the atrophic spots there was clinical evidence of papules interspersed with or

forming parts of the white spots, which suggested the clinical picture of lichen papules—as though either the white spot were an exaggerated form of the central depression or the central portion of a group of minute annular lesions that formed the periphery of the whole lesion. Histologically, there should appear elements suggestive of lichen planus and of skin atrophy, disappearance of the elastic tissue and sclerosis of the collagen. In this case, neither clinically nor histologically was there evidence of lichen albus, according to his impression of the condition. Clinically, this patient presented a large number of minute atrophic spots, a small macular anetoderma, if there was such a thing; in other words, a superficial punctate atrophy, not in the sense of classic macular idiopathic atrophy, but nevertheless a superficial atrophy. From the section presented, however, such a diagnosis could not be made, for although the papillary body was not well formed anywhere, this might normally be so at this site. Clinically, however, if there was such a thing as white spot disease, this was probably an example of it.

Dr. Wise said he had not had enough personal experience with these cases to speak intelligently about them; he had, however, read a great deal about them, and the best description he had seen was that by Ormsby in discussing lichen sclerosus and atrophicus. He regretted that he had injected the word lichen into the diagnosis. The correct diagnosis was not lichen albus of von Zumbusch, but dermatitis lichenoides chronica atrophicus. Dr. Williams had referred to the fact that there were no lichen planus papules, and he was right. The patient had not had lichen planus. Dr. Wise said he had seen six cases in which there was no suggestion of lichen planus. The only thing in this case that made him think of lichen planus was that the woman had papular lesions on the wrist; the history indicated that there had been no inflammatory papules. Dr. Wise agreed with Dr. Highman that it might be scleroderma in which the sclerous part of the change did not manifest itself to the naked eye, and with Dr. Williams that lichen was not a good name for the disease, even used as an adjective. If one looked at the patient in a good light, however, one could see lichenoid papules; and in the "Ikonographie Dermatologica" were two illustrations and a report of an eruption similar to this, and one that was shown two weeks ago under the name of dermatitis lichenoides chronica atrophicans.

A CASE FOR DIAGNOSIS. PITYRIASIS ROSEA OR TINEA CAPITIS?

Presented by Dr. Wise for Dr. Fordyce. (Previously presented at the April meeting of the Manhattan Dermatological Society.)

(Slide diagnosed as pityriasis rosea.)

DISCUSSION

Dr. Fordyce said he believed the case was one of pityriasis rosea with unusually large lesions. The clinical picture of pityriasis rosea was a varied one.

Dr. Schwartz agreed with the diagnosis.

Dr. Howard Fox agreed with the diagnosis, but said such a long duration was unusual; the fact that persistent searches for fungus had been negative was somewhat against the diagnosis of tinea. Furthermore, the eruption was profuse for tinea.

Dr. Wise said the small lesions were characteristic of pityriasis rosea, but as Dr. Fordyce had said, many of them were very large, and with such a long

duration the diagnosis of erythema multiforme ought to be considered, particularly as the papules on the chest were suggestive of erythema iris. Large circinate lesions in pityriasis rosea were not uncommon.

A CASE FOR DIAGNOSIS. (PIGMENTATION AND KERATOSIS OF THE PALM.) Presented by Dr. Howard Fox.

B. K., a mulatto woman, aged 24, born in the British West Indies, who had been in America for four years, had been married for two years, with one subsequent miscarriage eighteen months ago. She gave no other history suggestive of syphilis. The Wassermann test was four plus. She had received three intravenous injections of neo-arsphenamin. About ten or twelve years ago the patient first noticed a diffuse and mottled pigmentation covering the left palm. This condition remained unchanged until two years ago. Since that time the pigmentation had increased, and the process had spread to the present limits. The lesion was not improved by the injections of neo-arsphenamin. There was no history of the ingestion of arsenic or of other drugs. Examination revealed an eruption covering the entire left palm and the proximal third of the flexor surfaces of the fingers. The process had extended around the base of the thumb and involved the dorsal surfaces of the interdigital web between the thumb and forefinger. The lesion showed diffuse pigmentation, with many pea-sized, very dark brown spots scattered throughout. The borders were sharply demarcated. The palm showed mild hyperkeratosis.

DISCUSSION

Dr. Wise ventured the opinion that the condition was a nevus unilateralis.

Dr. Lane agreed with Dr. Wise that it was a nevus unilateralis.

Dr. Williams agreed with Dr. Wise and Dr. Lane, and told of another hereditary and usually congenital anomaly appearing late in life—that found in a man 40 years of age seen recently with keratotic lesions of the palms and soles. Looking at one palm or sole, one would say that it was hereditary keratosis, but it began after the age of 20 on one hand, and had not yet involved the middle of the palm. The man gave a distinct family history that his mother, younger brother and two children of a sister had the same condition, and, as in his case, it began long after birth. It seemed to be an hereditary deformity of the skin.

Dr. Bechet agreed with the diagnosis of nevus.

HYDROCYSTOMA. Presented by Dr. Wise for Dr. Fordyce.

Mrs. I. F., aged 63, born in Russia, had had the disease for fifteen years. On both cheeks and nose there were numerous small firm cystic elevations. A biopsy showed cystic dilatation of the sweat glands.

A CASE FOR DIAGNOSIS. Presented by Dr. Williams.

Mrs. A. K., aged 48, born in Hungary, three years ago developed an eruption on the hands said to be like that shown when presented; this disappeared after three months of treatment at Mount Sinai Hospital dispensary. Five months ago the present eruption began on the forearms, consisting of many soft papules, 1/16 inch (1.58 mm.) in diameter, scattered or arranged in cyclic patches. There were similar papules on the neck. On the right thigh there

was a patch 6 inches (15.24 cm.) in diameter, slightly brownish, with a slightly elevated red border. There was no pruritus and no sensory disturbance. A biopsy from the arm revealed: Epidermis showed normal thickness of the stratum mucosum; the basal cell layer was poorly defined in some places. Scattered through the derma were groups of small round cells. In some cases these were perivascular; in character they were largely mononuclears of the lymphocyte type. Ziehl-Neelson stain was negative for acid-fast bacilli, but scattered through the derma outside of the round cells were collections of cocci. These were also present in the sweat glands. The Wassermann test was negative.

DISCUSSION

DR. HIGHMAN remarked that if the observation as to the presence of organisms was correct and they were viable, the case might belong in the chronic erysipelas group, or be an example of erysipeloid of Rosenbach, and be due to transitory bacteremia from a cryptogenic focus, a focal infection; not a toxic eruption, but an actual bacterial invasion.

DR. FORDYCE said he considered the case clinically one of erythema perstans. The report that groups of organisms were found deep in the skin should be considered as a possible cause of the trouble. He cited a similar case which he had once seen in which streptococci had been demonstrated in the tissues.

CONGENITAL ALOPECIA. Presented by DR. WISE for DR. CLARK.

H. B., a boy, aged 4, Jewish, born in this country, presented two areas on the scalp, the size of silver dollars, on which the hair had never grown. The mother said that when the spots were first noticed the skin over the affected areas did not appear to be different from that on the rest of the scalp; but as the child grew older, the skin seemed to thicken. There had never been any subjective symptoms. At present, the child showed two areas on the crown entirely devoid of hair. There was slight scaling which appeared to be only usual exfoliation. The skin appeared to be thickened, and was loose and flabby, giving the impression on palpation of a lipomatous tumor. The parents refused to permit a biopsy.

PALMAR ERUPTION OF ERYTHEMA MULTIFORME TYPE FOLLOWING ARSPHENAMIN TREATMENT. Presented by DR. HOWARD FOX.

F. L., aged 26, a mulatto, was seen for the first time in January, 1923. At that time he presented a dime-sized indurated chancre of six days' duration, on the shaft of the penis. Dark-field examination showed the presence of *Spirochaeta pallida*. Treatment was instituted at the Harlem Hospital, and the patient received ten weekly injections. The first four were injections of sulpharsphenamin, and the last six were injections of neo-arsphenamin, a total of 1.58 gm. of the former and 2.7 gm. of the latter being given. Fifteen days after the last intravenous injection, the patient noticed an eruption on both palms, which was associated with considerable itching. Examination showed numerous discrete and confluent patches scattered over both palms. They were erythematous, sharply demarcated, round and gyrate in configuration, and varied in size from that of a pea to that of a dollar. There was no other eruption present on the body.

DISCUSSION

DR. FORDYCE said he had seen persistent localized scaling patches in patients who had received repeated injections of arsphenamin. In this connection, he referred to two cases of profound anemia following long intravenous administration of this substance. In both of these cases the red blood cells were below 2,000,000. In one of them the number of white cells was less than 2,000. The first patient completely recovered after several blood transfusions. The second patient died of a complicating pneumonia.

DR. LANE said he considered the case one of erythema multiforme, due to arsphenamin.

DR. WISE agreed with the diagnosis.

DR. HIGHMAN said it was an erythema multiforme, and might be due to arsphenamin; but what impressed him was the localization of the palms. This seemed to be an additional reason for ascribing it to the arsphenamin, in view of the known affinity of arsenic for the palms. Of course, arsphenamin eruptions occurred elsewhere on the body. It would be interesting to note whether this patient was developing palmar keratosis.

DR. HOWARD FOX said he believed that the erythema multiforme type of palm eruption might or might not be due to arsphenamin. At all events, he considered it an unusual clinical manifestation. He raised the question as to whether this should preclude further administration of arsphenamin.

DR. FORDYCE, replying to Dr. Fox's query, said he did not believe the condition of the palm should preclude further arsphenamin treatment. He had seen such lesions on other parts of the body in cases in which he continued to give arsphenamin. Dr. Fordyce said that in the Manchester epidemic, which occurred about 1900, it was a common observation to see patients with keratoses on the palms and soles. The patients came to the various clinics complaining of what they termed "tender feet."

DR. TRIMBLE said that if this were his patient, he would not give any more arsphenamin for a time, for fear the condition would advance.

PARAPSORIASIS EN PLAQUE. Presented by DR. WISE for DR. FORDYCE.

A, F., a man, aged 60, born in Austria, married, had had the skin disease for a year and a half. He had been treated by a number of physicians, and was presented by Dr. Levin at the last meeting of the Manhattan Dermatological Society. The patient presented a number of yellowish salmon colored plaques on the back chiefly, which were not scaly. There were evidences of itching. Urticaria was evident to-day in the clinic. A biopsy demonstrated the condition to be parapsoriasis.

DISCUSSION

DR. HIGHMAN said that neither clinically nor histologically was there anything to indicate that the condition was anything else, but that certainly these superficial infiltrations, although they showed none of the findings of mycosis except that they were sharply localized, gave no evidence against the fact that they might be precursors of that condition.

DR. WISE said they had been careful to warn the relatives that the patient must be carefully watched and examined at least once a month; for it might turn out to be a case of mycosis fungoides.

A CASE FOR DIAGNOSIS. Dr. Fordyce.

Dr. Fordyce showed a colored drawing of an unusual condition of the tongue which he had seen during the past winter. Two patients presenting almost identical diseases had come under his observation. In both of these cases there was a previous history of syphilis. The Wassermann tests, however, were negative when the patients were under his care, and antisyphilitic treatment had failed to influence the lesions. On the dorsum of the tongue there were a number of closely aggregated nodules, which were hard in consistency, and which showed no subjective sensation.

DISCUSSION

Dr. Highman said he had never seen such a case. Might it be summed up as a benign acanthoma of the tongue?

Dr. Trimble said he had never seen anything like it, but he had a vague recollection of having seen a colored photograph something like it in Butlin's book on tongue diseases.

Dr. Fordyce said the pathologic examination showed a marked acanthosis and a sclerosis of the underlying tissue.

MINNESOTA DERMATOLOGICAL SOCIETY

Regular Meeting, May 2, 1923

John M. Armstrong, M.D., *Presiding*

VASCULAR NEVUS. Presented by Dr. Michelson.

A man, aged 51, said that for the past thirty years he had had flat brownish-blue, sharply circumscribed areas scattered over his body; that they had enlarged slightly, and that they had caused him no inconvenience. On examination it was noted that there were about twenty such areas scattered over the body. The lesions had a distinct border, which was elevated. The border set the lesions off sharply from the surrounding skin. The center of each lesion seemed to be made up of dilated blood spaces, and with pressure some of the blood could be expressed. The patient refused a biopsy.

DISCUSSION

Dr. Michelson said that the diagnosis rested between a nevus and a morphea type of epithelioma. He said he did not believe a clinical diagnosis was possible, and he was sorry that the patient would not submit to a biopsy.

LICHEN URTICATUS. Presented by Dr. Klein.

A boy, 6 years of age, had measles on March 4; previous to this he had had a slight rash on the arms and forehead. Following the measles the rash became aggravated and itched considerably, and as a result the extensor surfaces of the arms and the skin on the forehead became covered with excoriations.

SYPHILIS RESEMBLING DERMATITIS HERPETIFORMIS. Presented by Dr. Armstrong.

A man, aged 44, married, two years ago had an eruption; the lesions were few until two months ago. Itching had been intense throughout the course of the trouble and more pronounced for the past two months. The patient contracted syphilis in 1917 and was treated with mercury and iodids continuously from the date of onset until the summer of 1922. He said that Wassermann tests were made in 1920, 1921 and 1922; the first positive and the last two negative. A Wassermann test was made today and was feebly positive. The lesion on the neck where his collar irritated was typically syphilitic, while the other lesions resembled a healing dermatitis herpetiformis. The pruritus was unusual in syphilis, and the picture as a whole was unusual.

SEBORRHEIC TYPE OF PSORIASIS. Presented by Dr. Michelson.

A woman, aged 34, was presented because of numerous circular, heavily scaled lesions, occurring throughout the hairy scalp. The scales were greasy and quite adherent. There was no dewdrop bleeding. There were a few papular lesions on the forehead, also on the back and chest. The knees showed typical psoriatic patches with mica-like scales.

DISCUSSION

Dr. Butler said he believed the scalp lesions were suggestive of seborrhea. The scales were loose and oily. The lesions on the knees looked like psoriatic lesions.

A CASE FOR DIAGNOSIS. Presented by Drs. Sweitzer, Michelson and Butler.

A woman, aged 72, presented a large circinate crusted and slightly ulcerated lesion over the right breast. She said that the disease had started three years before as a small pimple.

DISCUSSION

Dr. Michelson said that his diagnosis was dermatitis autophytica. He had closely questioned the patient, and she had given the following history: The first lesion she noticed appeared seven years before. It was a small nodule which she constantly picked at until crusts formed, which she removed almost every evening. The lesions became greatly enlarged, and because of her constant picking, healing was impossible.

Dr. Michelson said that they had been unable to obtain a Wassermann test. He thought she should be put in the hospital with an occlusion dressing, when observation should clear up the diagnosis.

TERTIARY SYPHILIS. Presented by Dr. Gager.

R. M., a colored man, aged 82, over large areas, on the left forearm and on the back had serpiginous syphilis with scarring and depigmentation of many years' duration. The patient had always been well until some days before, when he had had trouble with his eyesight. The Wassermann test was positive.

DISCUSSION

Dr. Sweitzer said he would diagnose the condition as psoriasis.

Dr. Butler said he believed Dr. Gager's diagnosis was right. He did not think it was psoriasis. There were large patches on the forearm, but no psoriatic scaling, and there was definite scarring. In negroes, there can be a depigmentation without much structural change in the skin.

Dr. Gager said he was positive it was a case of syphilis.

Dr. Michelson said that in his opinion this was a case of psoriasis vulgaris, and although the patient had a positive Wassermann reaction, he did not believe the lesions as presented were syphilitic.

URTICARIA PIGMENTOSA. Presented by Dr. Odland.

This case was reported at a previous meeting. The patient was presented for observation only.

DISCUSSION

Dr. Michelson said that he had made a biopsy. The section had been stained with Dominici stain and showed a dense infiltrate directly beneath the epidermis composed of pure mast cells, both the round and pointed variety.

PAPILLOMA OF THE LIP. Presented by Dr. Michelson.

A man, aged 31, had been sent to Dr. Michelson's clinic with a diagnosis of chancre of the lip. On examination a lesion the size of a dime was noted situated on the inner surface of the lower lip. The lesion was slightly elevated and had a distinct epithelial collar but no rolled edge. There was no ulceration, but the center semed to be verrucous. There were no palpable glands, and no dark-field examination had been made because chancre was ruled out clinically. Dr. Michelson's diagnosis was papilloma.

Note.—The growth was exicesd and sectioned, and the diagnosis of squamous cell epithelioma was made.

PITYRIASIS ROSEA. Presented by Dr. Odland.

A man, aged 35, had had the eruption for six weeks. The lesions were typical in morphology but unusually profuse and extensive on the face and generalized over the body and arms.

DISCUSSION

Dr. Armstrong said that the case was remarkable in the intensity of the eruption.

A CASE FOR DIAGNOSIS. (Probably an Erythema Menstruale.) Presented by Dr. Klein.

A girl, aged 14, had lesions which made their first appearance at the age of 8 and which appeared at intervals ever since. During the spring and fall months they were more prevalent. There was some improvement between the ages of 9 and 12, but at the time she began to menstruate the condition became aggravated, and during her periods the lesions became more prominent. Clinically the case resembled an erythema multiforme.

DISCUSSION

Dr. Gager said this girl had lesions typical of erythema, which fades on pressure. He thought the lesions looked exactly like erythema multiforme. The lesions on the face seemed to be fading out, and the patient was probably getting over one attack to have another.

NEUROTIC EXCORIATIONS. Presented by Dr. Klein.

A woman, aged 33, a housewife, said that ever since she was 11 years old she had had trouble with her skin. The condition became aggravated following a case of influenza three years before. Last August a kidney had been removed on account of pyonephrosis, and since then she had been rather nervous. She was given some bromids on account of this, but she had not taken any recently and did not notice that the rash grew worse following the taking of the medicine. When she reported to Dr. Klein there were many excoriations —old scars which were quite symmetrical and numerous pigmented areas.

DISCUSSION

Dr. Gager said that he believed a diagnosis of chronic urticaria with pigmentation should be considered.

Dr. Butler said he believed this was a case of Duhring's disease. There were grouped lesions on the thigh, polymorphic, pigmentation and scarring. He would rule out neurotic excoriations because in most patients the lesions are found where the patient can easily get at them.

Dr. Boreen said he favored Dr. Klein's diagnosis.

SECONDARY SYPHILIS. Presented by Dr. Gager.

E. T., a man, aged 30, unmarried, was first seen on April 10, 1923, presenting a balanitis with profuse discharge, and great edema of the foreskin for which a dorsal incision had been made. He returned on May 1 with a generalized eruption which was miliary in type, especially on the trunk on which minute vesicles were to be seen. The eruption in general was much more acutely red than is usual in syphilis. Diagnosis: secondary syphilis.

DISCUSSION

Dr. Butler said this was an interesting case. He said one reads about the vesicular syphilid but rarely sees it. This was one of the few cases he had ever seen, and he never before had seen one in this country.

D. D. Tunnicliff, Secretary.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, May 14, 1923

Fred D. Weidman, M.D., *Presiding*

DERMATITIS MEDICAMENTOSA WITH MOLLUSCUM CONTAGIOSUM. Presented by Dr. Strauss.

M. H., a white girl, aged 4 years, gave a history of an eruption which began about six months before. Three weeks before it had entirely disappeared, but another outbreak occurred. The child was seen by the presenter for the

first time on the day of the meeting. There was an indefinite history of taking cod liver oil and a "blood tonic." Quite a number of large pustules were present on the thighs and legs. On the neck and face were rather typical molluscum lesions. Atrophy occurred in some after three weeks. Small lesions began in the scalp following typical ones on the back of the neck. According to the history, they all started as molluscum tumors, but the pustules on the legs had all the appearance of a bromid exanthem.

DISCUSSION

DR. HIRSCHLER said he believed the main outbreak was a bromid eruption. This diagnosis was agreed on.

EPIDERMOLYSIS BULLOSA. Presented by DR. MUNSON.

J. K., a white girl, aged 10 years, presented bullous and crusted lesions in the axillae, on the back, arms and on one little finger. Such an eruption had been noticed since two weeks after birth. Any trauma caused an outbreak. If lifted under the arms the eruption appeared where the pressure had been exerted. The mother had never had a similar eruption, nor had any other member of the family.

PELLAGRA. Presented by DR. SCHAMBERG.

A negro woman, aged 42 years, born in the South but a resident of Philadelphia for many years, was first observed a few days previous to the meeting. She had applied strong mercuric chlorid solution to the hands, which might have produced a dermatitis, though in the strength used, 1:1,000, it was unusual to produce a condition of this kind. Further examination showed that she had a severe stomatitis with suggestive appearance of the tongue, which was beefy-red with pseudo-exudate on the side. There was marked salivation and a diarrhea of some weeks' standing. She had taken a variety of proprietary patent medicines. On the arms, from the elbows down, there was a severe dermatitis with superficial ulceration, bleeding and pigmentation and marked desquamation of the hands, with areas of superficial breaking. Bleb formation was not uncommon in pellagra. There were oval areas of pigmentation with roughening and epidermal thickening on the knees. The presenter said the patient had presented sufficient evidence to make the diagnosis of pellagra. She had been running a rise in termperature, 102.6 F., and was quite weak. The diet had always been varied. She had had no children and no miscarriages. The patient said that she had not known how to use the mercuric chlorid solution, but had rubbed it on her arms every morning and every night for nearly a week, for the relief of rheumatism. The pigmentation started about one month before, and had the appearance of being burned.

DISCUSSION

DR. HIRSCHLER asked about the state of the patient's mental condition.

DR. SCHAMBERG said he had not had sufficient time to look into that feature of the case. He believed this case was similar to the one reported by Dr. Fitzgerald of Boston, the first case of pellagra that was seen in New England. The picture of the hands was almost the counterpart of this. The history was somewhat obscure; the application of mercuric chlorid solution should not produce stomatitis.

DR. KNOWLES said he thought there was no question about the diagnosis.

DR. CORSON said he wished to know whether the patient had had a similar attack last year. Dr. Schamberg replied in the negative.

DR. WEIDMAN spoke of finding a hyperkeratosis in sections of a case brought to necropsy.

SYCOSIS BARBAE. Presented by DR. WEIDMAN.

J. R., a white man, aged 37 years, a presser on porcelain ware, presented a not unusual condition except that the upper lip was involved. A fungus cultivated from the upper lip proved to be *Trichophyton gypseum*. The condition was greatly improved under treatment. The patient was cut by a barber while being shaved, and the eruption subsequently developed on the chin and the left cheek.

NAPKIN ERUPTION (TWO CASES). Presented by DR. GREENBAUM.

E. N., a colored baby, aged 5 months, had a superficially ulcerated eruption on the buttocks, of one week's duration. The mother had a four plus Wassermann reaction, but the baby's Wassermann test was negative.

E. C., a white baby, aged 7 months, on admission to a hospital had had no disease of the skin, but developed an eruption after the second week there. He also had a rectal abscess. The skin lesions were rounded, crusted, superficial papules. A bleb had been the primary lesion. They had also appeared on the head.

DISCUSSION

DR. SCHAMBERG said he wished to know whether the lesions were not impetigo.

DR. KNOWLES said he thought it was a case of bullous impetigo, lesions being present on the scalp.

DR. GREENBAUM said that before the lesions became papular they were sometimes bullous, and later became ulcerated. He thought they corresponded to the napkin eruption of Jacquet, simulating syphilis.

DR. SCHAMBERG remarked that in regard to the white baby, he rather agreed with Dr. Knowles that the case did suggest impetigo, and he thought it quite possible that infection might occur from streptococci in the fecal contents. This particular child had a rectal abscess. Much depended on the virulence of the causative organism.

PIGMENTATION, CIRCUMORAL. Presented by DR. LUDY.

E. M., a white woman, aged 27 years, presented marked pigmentation around the mouth, the zone being about ⅛ inch (3.17 mm.) in breadth and of seven months' duration. The Wassermann test was negative. A history of using cosmetics was obtained.

CONGENITAL ALOPECIA. Presented by DR. LUDY.

J. B., a boy, aged 12 years, American born but of Italian parentage, was one of a family of six children—three boys and three girls. Two of the boys were similarly affected; the girls, however, had normal hair. This child had no hair until after the age of 7; at that time, dark and coarse hair developed, brittle and lifeless and sparsely covering the head.

DISCUSSION

DR. SCHAMBERG asked whether the patient perspired normally in the summer, and was told that he did.

DR. HIRSCHLER said he thought the appearance on the head was only part of a general condition seen on the skin although more characteristic in the former situation.

DR. SCHAMBERG said that the case presented a number of interesting features. The boy was inclined to be adipose and had rather a broad pelvis suggestive of pituitary dysfunction. There was a strong possibility of endocrine gland disturbance—most likely of the thyroid gland. He suggested that his sugar tolerance be taken. The features were certainly not masculine.

DR. KNOWLES said the boy had first been seen on the day of the meeting. Absence of certain secretions appeared most probable. There was prominence of follicles at the back of the head and in many regions on the trunk and the extremities.

DR. WEIDMAN said he thought it resembled a case previously shown by Dr. Drant. Some papules appeared inflammatory and some did not, more like a hyperplastic condition.

DR. KNOWLES suggested that the local action of some drug—such as tar—might have had some effect on the follicles.

GRANULOMA ANNULARE. Presented by DR. GREENBAUM.

C. W., a white man aged 29 years, had an eruption on the left hand of one and a half years' duration, and on the right hand of several months' standing. There was nothing in the mouth or on the genitalia to suggest lichen planus. No subjective symptoms were present. Rounded, but irregularly circular, clusters of pea-sized papules occurred on the dorsia of the hands.

DISCUSSION

DR. KNOWLES said the diagnosis seemed rather clear, but most cases showed a more definite ring form and clearing in the center.

DR. WEIDMAN agreed it was not typical. Usually these cases showed an abrupt rise on the outside of the ring, the inner slope being more gradual.

TELANGIECTASES. Presented by DR. HART-DRANT.

A white woman, aged 40, presented telangiectases on her upper arms and chest, of seven years' duration. The eruption first appeared at the beginning of an attack of hay-fever of the spring type, associated with violent paroxysms of sneezing and coughing; and the spots were noted to be worse at that time each year. The patient had a generally sensitive skin, formerly exhibiting a dermatitis which was thought to have been caused by dye from a fur. She had also eaten strawberries about the time of the eruption. She discarded the fur, but on eating strawberries a month later, the eruption promptly reappeared. As these angiomatous spots faded, they left pigmented areas. The coagulation time was one and one-half minutes; the blood count was practically normal and the urinalysis negative. Pigmented patches on the forehead appeared five months before. Pelvic examination showed a fibroid tumor. Dr. Hart-Drant said he thought the case fell in the same category as one recently shown by Dr. Weidman.

DISCUSSION

DR. WEIDMAN said he thought this case was similar to one shown by Dr. Arnett, though not nearly as marked. There were lesions forming short lines, consisting of large discrete telangiectases rather than petechial hemorrhages. From the section shown by Dr. Arnett, the conclusion was reached that some internal protein had, from time to time, exerted an influence on the lining of the terminal capillaries. Skin tests were tried without result. Dr. Arnett's patient was given injections of Coley's fluid and had a longer period of relief thereafter.

DR. SCHAMBERG said he regarded the case as one of multiple punctate telangiectases as the chairman stated. This condition might develop into a number of angiomas as the patient grew older.

LICHEN PLANUS HYPERTROPHICUS. Presented by DR. SMITH.

The patient was first seen on the day of the meeting and presented peculiar lesions on both legs and arms. There were purplish, flat papules and nodules and pigmented areas which had been present for six months. The patient also complained of itching. Roentgenograms had been made a week previously by Dr. Pfahler.

DISCUSSION

DR. SCHAMBERG said he thought the diagnosis was correct, and although many lesions on the legs were indistinguishable from prurigo, they were quite lichenoid on the flexor surface of the wrist where lichen planus was usually found.

DR. KNOWLES said he regarded the condition as unquestionably lichen planus.

SYPHILITIC MACULAR ATROPHY. Presented by DR. SIDLICK and DR. STRAUSS.

B. C., a negress, 27 years of age, presented pitted scars on the face, puffy scars on the trunk and red scaly patches on the legs. The latter was regarded as a relapsing eruption of syphilis. She first came to the clinic with an interstitial keratitis and a positive Wassermann reaction and had received active treatment for two years, including from thirty to forty injections of neoarsphenamin and ten or twelve injections of mercuric salicylate at weekly intervals. The blood and spinal fluid Wassermann tests were negative two weeks ago. Whenever treatment was relaxed, the eye became worse. There was in addition the question as to whether the appearance on the lower legs was due to arsenicals. The condition improved with treatment, the legs having been almost free at times, but when treatment was discontinued, the eruption reappeared.

DISCUSSION

DR. SCHAMBERG said the case was remarkable and presented a number of interesting features. In the first place, this girl at the age of 25 had an interstitial keratitis. He felt that the keratitis was the result of congenital syphilis. She showed an extensive flat, papulosquamous eruption on her legs, the scales looking quite like those of psoriasis and the lesions on the hands like lichen planus. Dr. Schamberg said he did not think the condition on the legs was syphilitic, but he thought it might be arsenical. The fact that the blood and spinal Wassermann tests were negative, was evidence against syphilis.

It would have to be assumed that she had become arsenic-fast and mercury-fast, and despite a negative Wassermann test, she had living spirochetes in her skin. After all the treatment she had received, the eruption would not have recurred like that.

Dr. Knowles said he thought the eruption was of the squamous type occurring on the palm. On a number of occasions, he had found this type difficult to clear up. Local applications were sometimes of assistance.

Dr. Strauss said he thought the condition might be tuberculous as in spite of a negative Wassermann test the eyes had again become inflamed, and the patient had difficulty in seeing.

A CASE FOR DIAGNOSIS. Presented by Dr. Weidman.

L. N., an Armenian girl, aged 13 years, had had acne vulgaris. There were four atrophic areas on the cheeks and forehead. Certain portions of the eruption consisted of marginated, translucent, red papules. This girl had been through Aleppo. The papules appeared to be inflammatory, and Dr. Weidman thought were closely related to sycosis. Although this patient was a girl, it was conceivable that such a thing as a folliculitis could exist.

DISCUSSION

Dr. Corson said he thought the case was identical with that of an Armenian girl shown at the previous meeting, except that the lesion was on the nose in that instance. She, herself, suggested Aleppo boil, having come from that region recently. The central portion had been destroyed by a caustic. In that case, it was diagnosed as lupus vulgaris. The case had been improved markedly in the last month by the roentgen-ray therapy.

Dr. Hirschler said he thought the case was one of lupus vulgaris

Dr. Knowles said he believed the diagnosis was correct.

BENIGN CYSTIC EPITHELIOMA. Presented by Dr. Corson.

H. G., a white man, aged 28 years, showed an eruption on the trunk which had been present since the age of 12 or 14, which began as one or two small tumors, gradually increasing in number until there are approximately 100 or more, some being elevated. A biopsy had been made and the section showed the cyst wall.

J. B. Ludy, Secretary.

Book Reviews

OLD RECOLLECTIONS OF AN OLD BOY. Samuel Sherwell, M.D. New York: Knickerbocker Press, 1923.

Sherwell's recollections are not like the recitals of the experiences of most medical men. Most of us lead commonplace existences. Unless a war happens to be thrown in, we go through life with the unexciting experiences of going to school, practicing medicine, and, maybe, teaching a bit and writing a bit. The autobiographies are often extremely interesting, particularly when they are genuine and frank, but they usually have nothing more adventurous to recount than a case of placenta praevia or a couple of years in Vienna. A few of us who have had the good luck to be in association with Dr. Sherwell have known that his early life was filled with more than ordinary adventure. But it will probably be a surprise to most readers to find the recollections of an old physician embodying the adventures that Sherwell had: Life in an English boarding school; across the Atlantic with Cyrus W. Field and Lord Kelvin on the *Niagara* when she was laying the first Atlantic cable; across the plains from the Missouri River to the Rocky Mountains, in 1860; with an ambulance corps in the Franco-Prussian War; in the oil fields of Pennsylvania in their early booming days—these are hardly the sort of experiences that you would expect in the life of a medical man. But Sherwell had a taste for seeing the world, and being of it. He was fortunately so situated that in his early life he could indulge the taste, and he accumulated an unusual store of interesting and solid experience. He confines the book to his early life in which these experiences occurred. It is regretted that he, who is so well known in dermatology, does not tell us more of his medical career beyond his two years in Vienna as a student.

Sherwell has a delightful personality, and something of it shows through the book. He is wise without being solemn or unbending; he has seen life through cheerful eyes; he has had more boyishness in him than is usual—and these things show in the book. One can almost hear his guttural voice and his good natured laugh as he tells his experiences. It is an interesting book, and he has been good to give it to us.

LECTURES ON DISEASES OF THE SKIN. Wallace Beatty, M.D., F.R.C.P.I., Physician to the Adelaide Hospital, Dublin; Honorary Professor of Dermatology, Trinity College, Dublin. Price, 15 shillings. Pp. 454. Dublin: Fannin & Co., Ltd.

This is a personal book, and, as such books usually are, when coming from first-rate men, is an interesting one. The book is written in an abbreviated, rather telegraphic style. The subjects are tabulated and carefully systematized. This book gives dermatology in a concentrated form, and it gives a great deal of information in a relatively small volume. This makes it a valuable reference book and book for students, but also a hard book to read except in brief parts. No one, no matter how experienced, can take the book up and read far without having his interest excited, and it is a

valuable reference book for any dermatologist. It would also be a useful book for students to use in connection with a more extensive reference book, or accompanying a lecture course.

PRACTICAL MEDICINE SERIES. VOL. VII. DERMATOLOGY AND SYPHILIS. Edited by WILLIAM ALLEN PUSEY and FRANCIS EUGENE SENEAR, Chicago: Year Book Publishing Co., 1922.

This year the volume appears with a change of editors. As usual, a section on genito-urinary diseases is included, edited by John H. Cunningham. A glance through the papers abstracted and critically reviewed reveals the choice of articles published during the year. Many probably did not come to the attention of the busy practitioner to whom the "Year Book" has a special appeal. The man interested in dermatology and syphilis will find the book a splendid manual for review or ready reference. Numerous plates illustrate the volume from pictures of the original articles. Despite the fact that most of the references are from American or English sources, numerous foreign language articles are included. This year, dermatology comprises about ninety pages, and syphilology about fifty more. These are illustrated by fifteen full page plates.

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